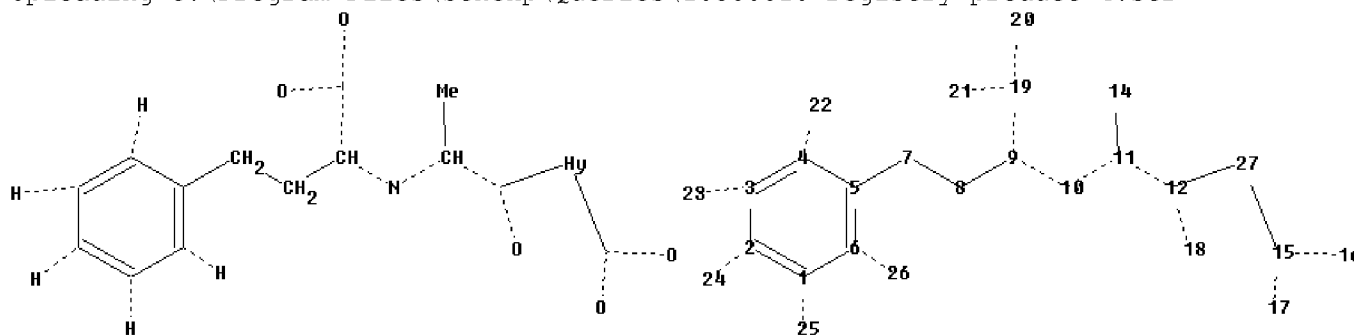


=>

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chain nodes :

7 8 9 10 11 12 14 15 16 17 18 19 20 21 22 23 24 25 26 27

ring nodes :

1 2 3 4 5 6

chain bonds :

1-25 2-24 3-23 4-22 5-7 6-26 7-8 8-9 9-10 9-19 10-11 11-12 11-14 12-18  
12-27 15-17 15-16 15-27 19-20 19-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-25 2-24 3-23 4-22 6-26 9-10 9-19 10-11 11-12 12-18 12-27 15-17 15-16  
15-27 19-20 19-21

exact bonds :

5-7 7-8 8-9 11-14

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS  
11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS  
20:CLASS 21:CLASS  
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:Atom

Generic attributes :

27:

Saturation : Saturated

Number of Hetero Atoms : Exactly 1

Type of Ring System : Polycyclic

L32 STRUCTURE UPLOADED

L32 STRUCTURE UPLOADED

L34 83 S L32 SSS FULL SUB=L18

FILE 'CAPLUS' ENTERED AT 10:01:13 ON 05 MAY 2008

L35 811 S L34

L36 111 S L35 AND SPN/RL

- ✓ L36 ANSWER 1 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Radioimaging moieties coupled to peptidase-binding moieties for imaging tissues and organs that express peptidases
- ✓ L36 ANSWER 2 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Methods and compositions of gene delivery to epithelial cells through bile acid peptide conjugate delivery agents for systemic and local therapy
- ✓ L36 ANSWER 3 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of pyrrolopyrimidines having Mnk1/Mnk2 inhibiting activity
- ✓ L36 ANSWER 4 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of 1-heterocyclylamino-2-hydroxy-3-amino- $\omega$ -arylalkanes as renin inhibitors for treating hypertension and other renin-mediated diseases
- ✓ L36 ANSWER 5 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ 6-(Aminoalkyl)indazoles as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
- ✓ L36 ANSWER 6 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Acylpiperidine compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
- ✓ L36 ANSWER 7 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Piperidinyl pyrrolidinyl methanone compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
- ✓ L36 ANSWER 8 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Thienopyrimidines having Mnk1/Mnk2 inhibiting activity for pharmaceutical compositions

✓ L36 ANSWER 9 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Piperidines and morpholines as renin inhibitors and their preparation,  
 pharmaceutical compositions and use in the treatment of diseases  
 associated with renin activity

✓ L36 ANSWER 10 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of substituted thiazolopyridines as PPAR modulators

✓ L36 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR  
 modulators

✓ L36 ANSWER 12 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Spiro imidazole derivatives as PPAR modulators and their preparation,  
 pharmaceutical compositions and use in the treatment of diseases  
 associated with PPAR activity.

✓ L36 ANSWER 13 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Oxazoles and thiazoles as PPAR modulators, their preparation,  
 pharmaceutical compositions, and use in therapy

✓ L36 ANSWER 14 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Oxazoles and thiazoles as PPAR modulators, their preparation,  
 pharmaceutical compositions, and use in therapy

✓ L36 ANSWER 15 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Oxazoles and thiazoles as PPAR modulators, their preparation,  
 pharmaceutical compositions, and use in therapy

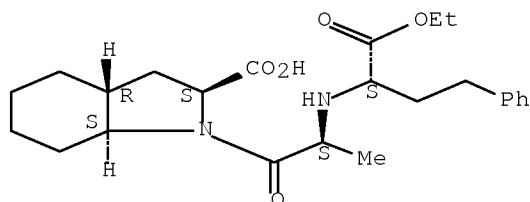
✓ L36 ANSWER 16 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Combination of a dipeptidyl peptidase-4 inhibitor and an anti-  
 hypertensive  
 agent for the treatment of diabetes and hypertension

✓ L36 ANSWER 17 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2007:397799 CAPLUS Full-text  
 DN 147:212296  
 TI Improved process for preparation oftrandolapril  
 IN Dattatraya, Patil Vishvas; Sharadrao, Varangaonkar Aniruddha  
 PA Torrent Pharmaceuticals Ltd., India

SO Indian Pat. Appl., 19pp.  
 CODEN: INXXBQ  
 DT Patent  
 LA English  
 FAN.CNT 1

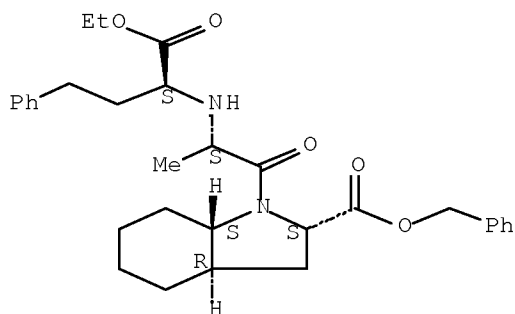
	PATENT NO.	KIND	√	DATE	APPLICATION NO.	DATE
PI	IN 2004KO00355	A		20060825	IN 2004-KO355	20040625
PRAI	IN 2004-KO355			20040625		
OS	CASREACT 147:212296					
AB	The invention discloses an improved process for the preparation of (2S,3aR,7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2-indolinecarboxylic acid, i.e., trandolapril. Key steps in the process include treating Me 3-chloro-N-acetylalanine with 1- pyrrolidinocyclohexene, followed by hydrolysis with 2N HCl and reductive cyclization over Pt/C to obtain 2β,3aβ,7aα-1H- octahydroindole-2-carboxylic acid hydrochloride. The N-benzoyl derivative was resolved via formation of the L-α-phenylethylamine salt.					
IT	87679-37-6F, Trandolapril RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (improved process for preparation of trandolapril)					
RN	87679-37-6 CAPLUS					
CN	1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)					

Absolute stereochemistry. Rotation (-).



IT 98677-37-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (improved process for preparation of trandolapril)  
 RN 98677-37-3 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ L36 ANSWER 18 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2007:388837 CAPLUS Full-text  
 DN 147:541727  
 TI Process for the preparation of trandolapril and intermediates thereof  
 IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu  
 Pattabhi; Bodkhe, Arjun Rajaram  
 PA Glenmark Pharmaceuticals Limited, India  
 SO Indian Pat. Appl., 31pp.  
 CODEN: INXXBQ  
 DT Patent  
 LA English  
 FAN.CNT 1  

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	IN 2004MU01060	A	✓ 20060728	IN 2004-MU1060	20041007
PRAI	IN 2004-MU1060		20041007		
OS	CASREACT 147:541727				
GI					

### **L36 ANSWER 19 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 2007:300486 CAPLUS Full-text  
 DN 147:522095  
 TI Process for the preparation of trans-octahydro-1H-indole-2-carboxylic acid  
 IN Debashish, Datta; Jagannath, Wani Mukesh  
 PA Lupin Ltd., India  
 SO Indian Pat. Appl., 37pp.  
 CODEN: INXXBQ  
 DT Patent  
 LA English  
 FAN.CNT 1  

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	IN 2003MU01033	A	20060120	IN 2003-MU1033	20031003
PRAI	IN 2003-MU1033		20031003		
OS	CASREACT 147:522095				
GI					

AB The invention relates to a process for the preparation of octahydroindole-2-carboxylic acid of formula I, wherein the ring junction is trans, including enantiomers, esters, and salts thereof, and more specifically (2S, 3aR, 7aS)-octahydro-1H-indole-2-carboxylic acid (II) and esters and salts thereof. Compound II is a valuable intermediate in the synthesis of the angiotensin converting enzyme (ACE) inhibitor trandolapril. The process of the invention avoids the use of expensive, hazardous, toxic, and corrosive chems., very low temps., and gives about 50% of the trans-isomer, making the process of the invention more com. attractive than prior art. The target compds. may be prepared according to the process of the invention as shown by the following example. Rhodium-catalyzed hydrogenation of the hydrochloride of imino acid III in water under alkaline conditions gave about 1:1 mixture of the trans- and cis-isomers of I. Fractional crystallization of the mixture from methanol resulted in the isolation of II and its enantiomer. Acetylation followed by diastereomeric salt formation with cinchonidine and acidification gave IV with 99.7% optical purity. Compound IV underwent deacetylation with hydrochloric acid to give II, which may be used to prepare trandolapril (V) in a single step.

IT 87679-37-6P, Trandolapril  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation);  
PREP (Preparation)  
    (target compound; process for preparation of trans-octahydro-1H-indole-2-carboxylic acid)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

√ L36 ANSWER 20 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI √ Nitric oxide enhancing angiotensin II antagonist compounds, and their  
preparation, compositions, and methods of use

√ L36 ANSWER 21 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2007:37921 CAPLUS Full-text  
DN 146:143003  
TI Process for the preparation oftrandolapril from N-[1-(S)-ethoxycarbonyl-3-  
phenylpropyl]-L-alanine N-carboxyanhydride and trans-octahydro-1H-indole-2-  
carboxylic acid.  
IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Phull, Manjinder

Singh; Sawant, Ashwini; Birari, Dilip Ramdas  
PA Cipla Limited, India; Curtis, Philip, Anthony  
SO PCT Int. Appl., 20 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2007003947	A2	20070111	WO 2006-GB2496	20060705
	WO 2007003947	A3	20070531		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
	IN 2005MU00793	A	20070601	IN 2005-MU793	20050705
	CA 2614099	A1	20070111	CA 2006-2614099	20060705
	EP 1899300	A2	20080319	EP 2006-755717	20060705
	R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRAI	IN 2005-MU793	A	√ 20050705		
	WO 2006-GB2496	W	20060705		

√ L36 ANSWER 22 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI √ Thienopyrimidines for pharmaceutical compositions and their preparation and use as kinase inhibitors

## **L36 ANSWER 23 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 2006:1339720 CAPLUS Full-text  
DN 146:82189  
TI Preparation of L-threonine derivatives with high therapeutic index  
IN Chandran, V. Ravi  
PA USA  
SO U.S. Pat. Appl. Publ., 60pp., Cont.-in-part of U.S. Ser. No. 343,557.  
CODEN: USXXCO

DT Patent  
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 20060287244	A1	20061221	US 2006-442027	20060526
	WO 2005046575	A2	20050526	WO 2004-US24901	20040729
	WO 2005046575	A3	20071004		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,			

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

US 20060241017 A1 20061026 US 2006-343557 20060130

PRAI US 2003-491331P P 20030729

WO 2004-US24901 A2 20040729

US 2006-343557 A2 20060130

AB The invention is directed to novel therapeutic compds. comprised of an L-threonine bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties, with the addnl. advantage of separating various enantiomeric and diastereomeric drugs into their individual isomers. The examples describe the synthesis and activities of L-threonine derivs. of (±)- and (+)-(S)-ibuprofen, (±)- and (+)-(S)-ketoprofen, (-)-(S)-ketorolac, aspirin, and fenofibric acid. The synthesis and activity of several L-serine and L-hydroxyproline analogs were also described. Thus, the hydrochloride of (+)-(S)-ibuprofen ester of L-threonine was prepared, and its free base examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.

IT 917472-72-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-threonine derivs. with high therapeutic index)

RN 917472-72-1 CAPLUS

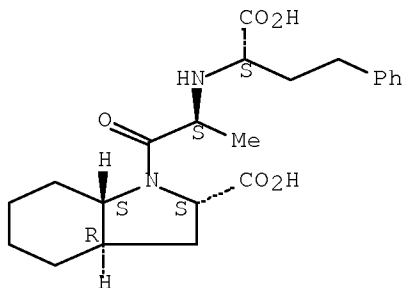
CN L-Threonine, ester with (2S,3aR,7aS)-1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (CA INDEX NAME)

CM 1

CRN 87679-71-8

CMF C22 H30 N2 O5

Absolute stereochemistry.



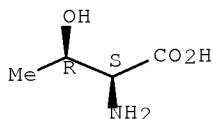


CM 2

CRN 72-19-5

CMF C4 H9 N O3

Absolute stereochemistry.



IT 87679-71-8, Trandolaprilat

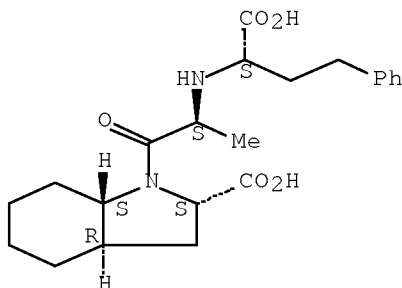
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of L-threonine derivs. with high therapeutic index)

RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ L36 ANSWER 24 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI ✓ Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes

✓ L36 ANSWER 25 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI ✓ Preparation of 4-biarylyl-1-phenylazetidin-2-ones for the treatment of hypercholesterolemia

✓ L36 ANSWER 26 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1222092 CAPLUS [Full-text](#)

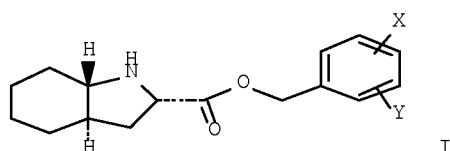
DN 146:7821

TI Process for the preparation of (2S,3aR,7aS)-octahydroindole-2-carboxylates and their conversion to trandolapril

IN Akhtar, Haider; Ramesh, Babu Potluri; Venkata, Subhramanian

Hariharakrishnan; Hari, Prassad Kodali  
 PA Sochinaz SA, Switz.  
 SO Eur. Pat. Appl., 19pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1724260	A1	✓ 20061122	EP 2005-76060	20050506
	EP 1724260	B1	20080220		
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
	AT 386718	T	20080315	AT 2005-76060	20050506
PRAI	EP 2005-76060	A	20050506		
OS	CASREACT 146:7821; MARPAT 146:7821				
GI					



AB A process for preparation of benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide (I; X, Y = H, halo, alkyl, alkoxy), and its conversion to trandolapril comprises (a) reaction of Me  $\beta$ -hydroxyalaninate hydrochloride with an acylating agent in a nonpolar solvent to give a diacylated derivative, (b) reaction of the latter with a cyclohexanone enamine to give Me N-acyl- $\beta$ -(2-oxocyclohexyl)alaninate, (c) hydrolytic cyclization to give an indole, (d) hydrogenation to a perhydroindole derivative, (e) esterification with a benzyl alc. followed by conversion of the benzyl ester arylsulfonate to the hydrohalide I, (f) resolution and conversion to a benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide, and (g) coupling with ECPPA (N-[(1-ethoxycarbonyl)-3-phenylpropyl]-(S)-alanine) acid chloride hydrochloride and debenzylating hydrogenolysis.

✓ L36 ANSWER 27 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ 4-Biaryllyl-1-phenylazetidin-2-one glucuronide derivatives for hypercholesterolemia

## **L36 ANSWER 28 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 2006:1124123 CAPLUS Full-text  
 DN 145:455276  
 TI Preparation of amino acid derivatives with high therapeutic index  
 IN Chandran, V. Ravi  
 PA USA

SO U.S. Pat. Appl. Publ., 139pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20060241017	A1	20061026	US 2006-343557	20060130
	WO 2005046575	A2	20050526	WO 2004-US24901	20040729
	WO 2005046575	A3	20071004		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA			
	US 20060287244	A1	20061221	US 2006-442027	20060526
	WO 2007089745	A2	20070809	WO 2007-US2475	20070129
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
PRAI	US 2003-491331P	P	20030729		
	WO 2004-US24901	A2	20040729		
	US 2006-343557	A2	20060130		

AB The invention is directed to novel therapeutic compds. comprised of an amino acid bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties. The examples describe the synthesis and activities of amino acid derivs. of propofol, ibuprofen, ketoprofen, ketorolac, aspirin, acetaminophen, cyclosporin A, valproic acid, clopidogrel, damazol, benzapril, enalapril, and fenofibric acid. Thus, ( $\pm$ )-ibuprofen esters of L-serine, L-threonine, and L-hydroxyproline were prepared and examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.

IT 87679-71-8, Trandolaprilat

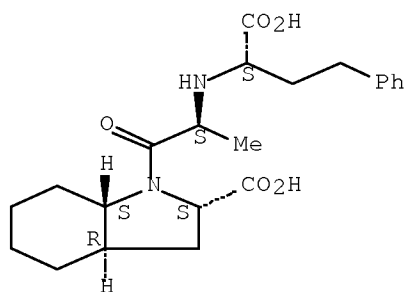
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(preparation of amino acid derivs. with high therapeutic index)

RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



√ L36 ANSWER 29 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Organic nitric oxide enhancing salts of angiotensin II antagonists, compositions and methods of use

√ L36 ANSWER 30 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Preparation of nitric oxide enhancing diuretic compounds, compositions and methods of use

√ L36 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2006:818063 CAPLUS Full-text  
 DN 145:211348  
 TI Improved process for preparation of highly pure trandolapril  
 IN Singh, Girij Pal; Wani, Mukesh Jagannath; Lande, Hemraj Mahadeorao; Jain, Adinath Murlidhar  
 PA Lupin Limited, India  
 SO PCT Int. Appl., 34pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006085332	A1	20060817	WO 2005-IN301	√ 20050906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM

IN 2005MU00155	A	20060908	IN 2005-MU155	20050214
AU 2005327440	A1	20060817	AU 2005-327440	20050906
EP 1866327	A1	20071219	EP 2005-823818	20050906

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRAI IN 2005-MU155 A 20050214  
WO 2005-IN301 W 20050906

OS CASREACT 145:211348

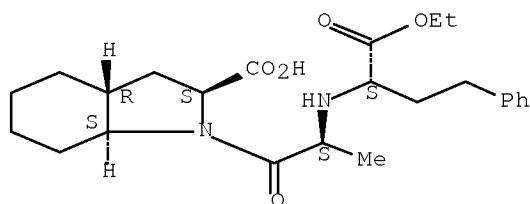
AB Highly puretrandolapril was prepared by acylation of benzyl trans-(2S,3aR,7aS)-octahydro-1H-indolecarboxylate [(2S,3aR,7a)-I] with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride, followed by crystallization from appropriate solvents. (2S,3aR,7a)-I was prepared by (1) crystallization of a mixture of racemic I tosylates (2S,3aR,7aS and 2R,3aS,7aR) to enrich the purity to >99% from a mixture containing the cis diastereomers up to 6 %, (2) optical resolution of the racemic mixture of (2S,3aR,7aS)- and (2R,3aS,7aR)-I with (-)-dibenzoyl-L-tartaric acid monohydrate, (3) reaction of the tartrate salt with N-[1-(S)- ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride to givetrandolapril benzyl ester, and crystallization of crudetrandolapril. Trandolapril obtained by this process had HPLC purity 99.94% and a characteristic X-ray powder diffraction pattern.

IT 87679-37-6P, Trandolapril  
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(X-ray powder diffraction; preparation of highly puretrandolapril)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

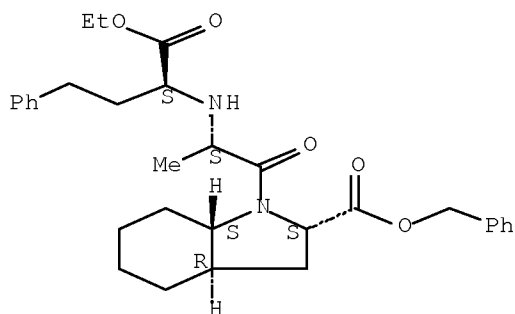


IT 98677-37-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of highly puretrandolapril)

RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L36 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Hydroxylated nebivolol metabolites for treating and/or preventing  
vascular  
diseases

✓ L36 ANSWER 33 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ 1-Acylamino-2-hydroxy-3-amino-w-arylalkanes as renin inhibitors and  
their  
preparation, pharmaceutical compositions and their use for treatment of  
hypertension

✓ L36 ANSWER 34 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of 4-  
[(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyaceti  
c acids as PPAR modulators

✓ L36 ANSWER 35 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of pyrazolopyrimidines as inhibitors of kinase activity

✓ L36 ANSWER 36 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Diuretic compounds comprising heterocyclic nitric oxide donor groups,  
compositions and methods of use

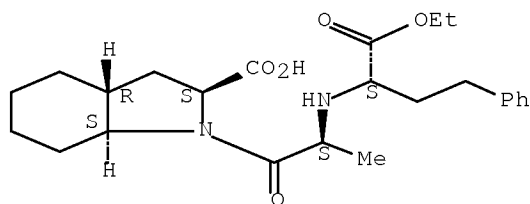
✓ L36 ANSWER 37 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Nitrosated and nitrosylated compounds, compositions, and methods for

the  
treatment of ophthalmic disorders

✓ L36 ANSWER 38 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:341506 CAPLUS Full-text  
DN 144:350983  
TI Process for the preparation of (2S,3aR,7aS)-perhydroindole-2-carboxylic  
acid intermediate in synthesis of trandolapril  
IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu  
Pattabhi; Bodkhe, Arjun Rajaram  
PA Glenmark Pharmaceuticals Limited, India  
SO U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 20060079698	A1	20060413	US 2005-245871	20051007
PRAI	US 2004-616934P	P	✓ 20041007		
	US 2004-616959P	P	20041007		
OS	CASREACT 144:350983; MARPAT 144:350983				
AB	Trandolapril intermediate (2S,3aR,7aS)-perhydroindole-2-carboxylic acid was prepared by a process which comprises esterification of (3aR,7aS)-perhydroindole-2-carboxylic acid with an alc. in the presence of an acid, reacting the acid addition salt with a base and then dibenzoyl-L-tartaric acid or di-p-toluoyl-L-tartaric acid and at least one alc., followed by addition of a second base and hydrolysis. (2S,3aR,7aS)-perhydroindole-2-carboxylic acid prepared by this method was used to prepare trandolapril.				
IT	87679-37-6P, Trandolapril RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of perhydroindolecarboxylic acid intermediate in synthesis of trandolapril)				
RN	87679-37-6 CAPLUS				
CN	1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)				

Absolute stereochemistry. Rotation (-).



✓ L36 ANSWER 39 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of bicyclic anilide spirolactam cgrp receptor antagonists

√ L36 ANSWER 40 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI √ Preparation of tricyclic anilide spirohydantoin CGRP receptor antagonists

√ L36 ANSWER 41 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2006:119252 CAPLUS Full-text  
DN 144:171268  
TI Preparation of trandolapril  
IN Reddy, Pratap Padi; Chitre, Saurabh Shashikant; Polavarapu, Srinivas; Vakamudi Sri Naga Venkata Laxmi, Varaprasad  
PA Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.  
SO PCT Int. Appl., 21 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2006014916	A2	20060209	WO 2005-US26423	20050726
	WO 2006014916	A3	20060803		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	IN 2007CN00572	A	20070824	IN 2007-CN572	20070208
PRAI	US 2004-591035P	P	√ 20040726		
	US 2004-607839P	P	20040908		
	WO 2005-US26423	W	20050726		

OS CASREACT 144:171268  
AB The invention relates to a process for preparing trandolapril, (2S,3aR,7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2-indolinecarboxylic acid, and intermediates formed in the process. Thus, (±)-benzyl octahydro-2-indolecarboxylate hydrochloride was treated with N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanine in CH<sub>2</sub>Cl<sub>2</sub> in the presence of hydroxybenzotriazole and dicyclohexylcarbodiimide at 20-25°C for 3 h. Hydrogenation over 10% Pd on charcoal and workup, including recrystn., afforded trandolapril.

√ L36 ANSWER 42 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI √ Thiazole compounds as PPAR modulators, their preparation, pharmaceutical



compositions, and use in therapy

✓ L36 ANSWER 43 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Oxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

✓ L36 ANSWER 44 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

✓ L36 ANSWER 45 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

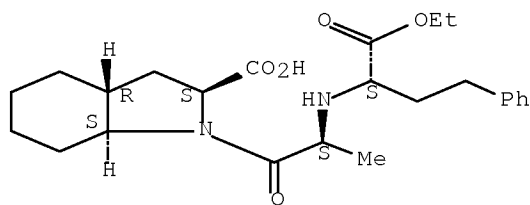
✓ L36 ANSWER 46 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Combination of (S)-amlodipine and an ACE inhibitor for reducing hypertension

✓ L36 ANSWER 47 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics.

✓ L36 ANSWER 48 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Nitric oxide-releasing pyruvate compounds, compositions and methods for treating cardiovascular and other diseases

✓ L36 ANSWER 49 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - INSTANT

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005054194	A1	20050616	WO 2004-EP13377	20041125
	US 20070225505	A1	20070927	US 2007-580610	20070212
PRAI	EP 2003-257417	A	20031125		
	WO 2004-EP13377	W	20041125		



✓ L36 ANSWER 50 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2005:493585 CAPLUS Full-text  
 DN 143:32341  
 TI Method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S,  
 3aR, 7aS-octahydroindol-2-carboxylic acid} compounds especially  
 trandolapril via their racemic salts  
 IN Poguttor, Mirko; Rudolf, Felix; Bichsel, Hans-Ulrich; Bader, Thomas  
 PA Azad Pharmaceuticals Ingredients A.-G., Switz.  
 SO PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA German  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051909	A1	20050609	WO 2004-CH688	✓ 20041115
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1689711	A1	20060816	EP 2004-797245	20041115
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			
	JP 2007512260	T	20070517	JP 2006-540130	20041115
	IN 2006KN01385	A	20070504	IN 2006-KN1385	20060523
	US 20070135513	A1	20070614	US 2007-580638	20070208
PRAI	CH 2003-2038	A	20031128		
	WO 2004-CH688	W	20041115		

AB The invention relates to a method for producing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} and the pharmaceutically acceptable salts thereof. To this end, a racemic mixture of optionally substituted trans-octahydroindol-2-carboxylic acid is reacted with the N-carboxyanhydride of {N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine}, which is optionally substituted on the Ph ring, in an appropriate inert solvent, and the obtained optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid}, preferably trandolapril, is subsequently isolated, as well as polymorphous forms A and B of trandolapril.

✓ L36 ANSWER 51 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of nitrosated glutamic acid compounds for use in  
 pharmaceutical compositions

✓ L36 ANSWER 52 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of biphenyl or phenylheterocyclyl moiety-containing esters  
 as inhibitors of microsomal triglyceride transfer protein

✓ L36 ANSWER 53 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ 2'-Benzothiazolylthioesters of N-substituted alpha amino acids:  
 versatile intermediates for synthesis of ACE inhibitors  
 SO ✓ Synthetic Communications (2005), 35(2), 243-248

✓ L36 ANSWER 54 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Nitrosated and nitrosylated cardiovascular compounds, their  
 compositions,  
 and use

✓ L36 ANSWER 55 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of benzodiazepine derivatives as CGRP receptor antagonists

✓ L36 ANSWER 56 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of phosphorus-containing rapamycin derivatives for use in  
 pharmaceutical compositions as immunosuppressive and anticancer agents

✓ L36 ANSWER 57 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives  
 as agonists for the RUP25 nicotinic acid receptor for the treatment of  
 dyslipidemia and related diseases

✓ L36 ANSWER 58 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of  $\alpha$ -amino acid benzothiazolylthio esters as  
 intermediates for manufacture of ACE inhibitors

√ L36 ANSWER 59 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Preparation of benzodiazepine CGRP receptor antagonists

√ L36 ANSWER 60 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Enalapril-nitroxy derivatives and related compounds as ace inhibitors  
 for

the treatment of cardiovascular diseases

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110432	A1	20041223	WO 2004-EP51089	20040611
PRAI	EP 2003-101796	A	20030619		
	WO 2004-EP51089	W	√ 20040611		

√ L36 ANSWER 61 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Process for the preparation of enalapril maleate and related compounds  
 having ACE inhibitory action

IN Jenko, Branko  
 PA Lek Pharmaceuticals D.D., Slovenia

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004101515	A1	20041125	WO 2004-SI21	√ 20040507
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	SI 21507	A	20041231	SI 2003-123	20030516
	EP 1628956	A1	20060301	EP 2004-731808	20040507
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 20070072919	A1	20070329	US 2006-556986	20060929
PRAI	SI 2003-123	A	20030516		
	WO 2004-SI21	W	20040507		

√ L36 ANSWER 62 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:931415 CAPLUS Full-text

DN 141:366125  
 TI Preparation of trandolapril from diastereomeric salt of benzyl  
 (2S,3aR,7aS)-hexahydro-2-indolinecarboxylate  
 IN Shimamura, Hiroshi  
 PA Ohara Pharmaceutical Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 8 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	JP 2004307340	A	√ 20041104	JP 2003-73056	20030318
PRAI	JP 2003-37749	A	20030217		

AB Trandolapril (I) is prepared by amidation of benzyl (2S,3aR,7aS)-hexahydro-2-indolinecarboxylate (II) salt with optically active 10-camphorsulfonic acid, with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine or its N-carboxyanhydride (III) in tertiary amine-containing solvent, followed by hydrogenolysis of the resulting amide benzyl ester. Thus, II.(1R)-(-)-10-camphorsulfonate was amidated with III in DMF in the presence of Et<sub>3</sub>N, then hydrogenated over Pd/C to give I with 82% total yield.

√ L36 ANSWER 63 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Preparation of azole compounds as PTP1B inhibitors

√ L36 ANSWER 64 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Evaluation of adsorption and penetration of angiotensin converting enzyme inhibitor, trandolapril, and its active metabolite, trandolaprilate, to the dialysis membrane  
 AU Zaitzu, Kiyoshi; Hamase, Kenji; Hayashi, Hiromi; Nagayasu, Reiko; Fukuda, Hiroko; Tomita, Tatsunosuke; Morikawa, Akiko  
 CS Graduate School of Pharmaceutical Sciences, Kyushu University, Japan  
 SO √ Igaku to Yakugaku (2004), 51(6), 843-849  
 CODEN: IGYAEI; ISSN: 0389-3898

√ L36 ANSWER 65 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - CHECKED DOC  
 TI Novel crystalline forms of trandolapril

√ L36 ANSWER 66 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2004:633914 CAPLUS Full-text  
 DN 141:140316  
 TI Process for producing intermediate for trandolapril by esterification of racemic (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid with benzyl alcohol and optical resolution  
 IN Shimamura, Hiroshi; Nakata, Yoshitaka

PA Ohara Chemical Industries, Ltd., Japan  
SO PCT Int. Appl., 15 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004065368	A1	√ 20040805	WO 2004-JP374	20040119
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				

√ L36 ANSWER 67 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2004:605707 CAPLUS Full-text  
DN 141:117164  
TI Preparation of (2S,3aR,7aS)-1-[(S)-N-[(S)-1-ethoxycarbonyl-3-phenylpropyl]alanyl]hexahydro-2-indolinecarbon acid benzyl ester as an antihypertensive agent  
IN Shimamura, Hiroshi  
PA Ohara Yakuhin Kogyo K. K., Japan  
SO Jpn. Kokai Tokkyo Koho, 6 pp.  
CODEN: JKXXAF

DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2004210660	A	√ 20040729	JP 2002-379498	20021227
PRAI	JP 2002-379498		20021227		
AB	The title compound, Trandolapril benzyl ester, was prepared by reaction of (2s,3aR,7aS)-hexahydro-2-indolinecarbon acid benzyl ester with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl-N-carboxy anhydride as an antihypertensive agent.				

√ L36 ANSWER 68 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - CHECKED DOC  
AN 2004:490720 CAPLUS Full-text  
DN 141:59698  
TI ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders  
IN Haj-Yehia, Abdullah Ibrahim; Khan, Mohamed Amin; Qadri, Bashir Ali  
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel  
SO PCT Int. Appl., 91 pp.  
CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004050084	A2	20040617	WO 2003-IL1006	20031127
	WO 2004050084	A3	20040930		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003286389 A1 20040623 AU 2003-286389 20031127  
EP 1578413 A2 20050928 EP 2003-777134 20031127

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 20060166894 A1 20060727 US 2005-536628 20051219

PRAI US 2002-429864P P 20021129  
US 2002-430003P P 20021129  
WO 2003-IL1006 W 20031127

OS MARPAT 141:59698

AB The present invention provides multifunctional ACE inhibitor compds. that combine ACE-inhibiting activity with capability to scavenge superoxide and other reactive oxygen species, and that may further function as nitric oxide (NO) donors. The compds. are useful for preventing or treating various disorders, including cardiovascular, and diabetes-associated disorders. This invention is further directed to a method for treating and preventing a disorder in which treatment with an ACE inhibitor is indicated, and mainly cardiovascular disorders, renal disorders, and diabetes-associated disorders. The use of said compds. in the preparation of a medicament is further provided.

√ L36 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

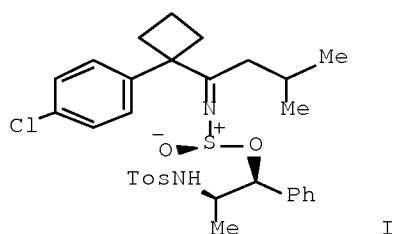
TI √ Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders

√ L36 ANSWER 70 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI √ Preparation of N-phenyl or N-heterocyclyldibenzylamine compounds as inhibitors of cholesteryl ester transfer protein (CETP) and medicinal use thereof

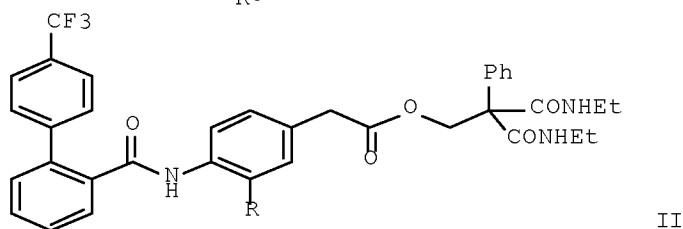
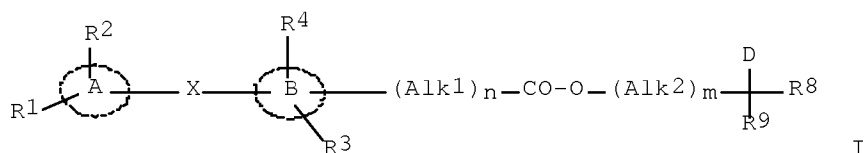
√ L36 ANSWER 71 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI √ Method of preparing amine stereoisomers via reduction of sulfinylimines in presence of chiral auxiliaries



✓ L36 ANSWER 72 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI ✓ Preparation of [4-(1,1'-biphenyl-2-ylcarbonylamino or benzoylamino)phenyl]acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors



✓ L36 ANSWER 73 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI MV Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor

## **L36 ANSWER 74 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 2003:255129 CAPLUS [Full-text](#)

DN 138:271979

TI Method for producing enalapril and related angiotensin converting enzyme inhibitors

IN Tien, Mong-Jong; Liu, Yu-Liang

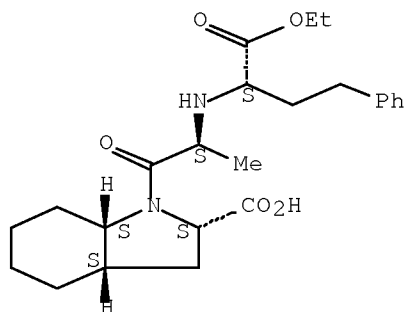
PA Everlight USA, Inc., USA



SO U.S., 7 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6541635	B1	20030401	US 2002-178369	20020625
PRAI	TW 2002-91106399	A	20020329		
OS	CASREACT 138:271979				
AB	The invention discloses a method for producing angiotensin converting enzyme inhibitors (S)-PhCH <sub>2</sub> CH <sub>2</sub> CH(CO <sub>2</sub> Et)-L-Ala-R (NEPA-R) and pharmaceutically-acceptable salts via deprotection of carboxy group-protected derivs. in non-aqueous medium. The product is obtained in high yield with minimal byproduct formation. Thus, NEPA-L-Pro-OSiMe <sub>3</sub> , prepared by coupling of NEPA-NCA with H-L-Pro-OSiMe <sub>3</sub> , was stirred with isopropanol at room temperature and treated with maleic acid to afford 87.1% enalapril maleate.				
IT	80876-01-3P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)				
RN	80876-01-3 CAPLUS				
CN	1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)				

Absolute stereochemistry.

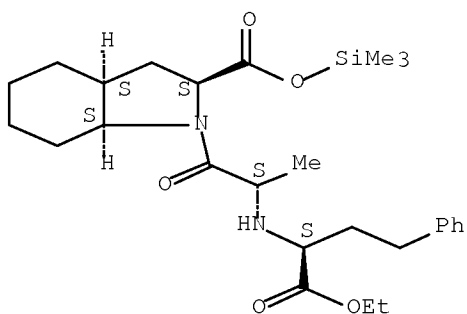


IT 503322-60-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)

RN 503322-60-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

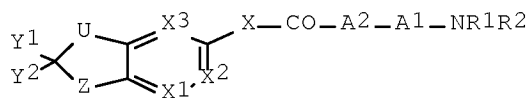
Absolute stereochemistry.



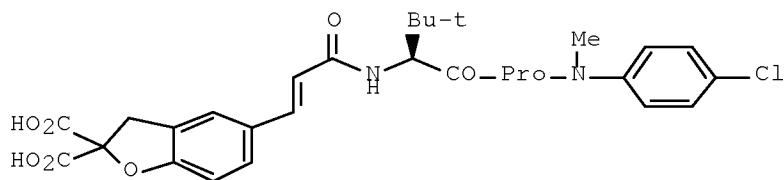
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L36 ANSWER 75 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Compositions comprising a polypeptide and an active agent

✓ L36 ANSWER 76 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of peptides as STAT modulators



I



II

✓ L36 ANSWER 77 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Compositions comprising a polypeptide and an active agent

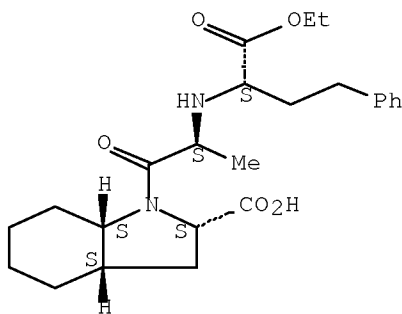
✓ L36 ANSWER 78 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation of amino acid salts soluble in organic solvents and their  
use in dipeptide synthesis

√ L36 ANSWER 79 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI √ Cobalamin compounds useful as cardiovascular agents and as imaging agents

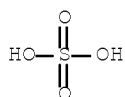
**L36 ANSWER 80 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 2001:880052 CAPLUS Full-text  
DN 136:279663  
TI Procedure for the synthesis of ACE-inhibitors  
AU Coll, Alberto Palomo; Morte, Sonia Serra  
CS Centro Genesis para la Investigacion, S. L., Barcelona, 08021, Spain  
SO Afinidad (2001), 58(495), 391-393  
CODEN: AFINAE; ISSN: 0001-9704  
PB Asociacion de Quimicos del Instituto Quimico de Sarria  
DT Journal  
LA Spanish  
OS CASREACT 136:279663  
AB A new simple and economic synthesis of Enalapril maleate and Trandolapril sulfate in 85% yield is described.  
IT 406218-99-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of ACE-inhibitors)  
RN 406218-99-3 CAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, sulfate (2:1) (CA INDEX NAME)  
  
CM 1  
  
CRN 80876-01-3  
CMF C24 H34 N2 O5

Absolute stereochemistry.



CM 2  
  
CRN 7664-93-9  
CMF H2 O4 S

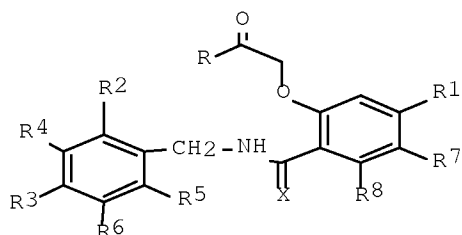


RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L36 ANSWER 81 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ STAT4 and STAT6 binding dipeptide derivatives

✓ L36 ANSWER 82 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Synthesis, activity and formulations of pharmaceutical compounds for  
treatment of oxidative stress and/or endothelial dysfunction

✓ L36 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Preparation and effect of Substituted phenoxyacetic acids in  
complications  
arising from diabetes mellitus



I

✓ L36 ANSWER 84 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Synthesis, activity and formulations of pharmaceutical compounds for  
treatment of oxidative stress and/or endothelial dysfunction

✓ L36 ANSWER 85 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
TI ✓ Synthesis, activity and formulations of pharmaceutical compounds for  
treatment of oxidative stress and/or endothelial dysfunction

√ L36 ANSWER 86 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease

## **L36 ANSWER 87 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1999:705055 CAPLUS Full-text

DN 131:322920

TI Process for preparing N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives

IN Yang, Suh-Wan; Chang, Yu-An; Liu, Yu-Liang

PA Everlight USA, Inc., USA

SO U.S., 6 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 5977380	A	19991102	US 1999-251341	19990217

PRAI US 1999-251341 19990217

OS CASREACT 131:322920; MARPAT 131:322920

AB (S)-EtO<sub>2</sub>CCCH(CH<sub>2</sub>CH<sub>2</sub>Ph)-Ala-R (I; R are certain cyclic amino acids, e.g., L-proline) or their pharmaceutically acceptable salts were prepared by coupling I (R = OC<sub>6</sub>H<sub>4</sub>R<sub>1</sub>, where R<sub>1</sub> is nitro, cyano, sulfite, carboxy, aldehyde, ester, or halo) with an amino acid. Thus, I (R = OC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-p), formed by esterifying the acid with 4-nitrophenol in the presence of triethylamine and thionyl chloride in dichloromethane, was treated with L-proline to afford I (R = proline residue) (enalapril).

IT 80876-01-3P

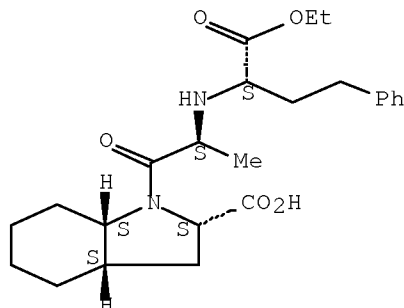
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5        THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

**L36    ANSWER 88 OF 111    CAPLUS    COPYRIGHT 2008 ACS on**

STN

AN 1998:38475 CAPLUS Full-text

DN 128:61791

TI Method for the production of L-alanine derivatives with an ACE inhibitor effect

IN Palomo Coll, Alberto; Serra Mortes, Sonia

PA KRKA Tovarna Zdravil D. D., Slovenia

SO Ger. Offen., 6 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	DE 19721290	A1	19971211	DE 1997-19721290	19970521
PRAI	SI 1996-169	A	19960522		

OS MARPAT 128:61791

AB Title compds. R1CH2CH2CH(CO2Et)NHCH(CH3)COR2 [(I): R1 = alkyl, aryl, heterocycle; R2 = (un)natural  $\alpha$ -amino acid], and their pharmaceutically acceptable salts were prepared as ACE-inhibitors (no data). Thus, (S,S)-I (R1 = Ph; R2 = OH) was reacted with L-proline to yield (S,S)-I (R1 = Ph; R2 = L-proline), which was converted to its maleate salt.

IT 87679-37-6P 200423-23-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation);

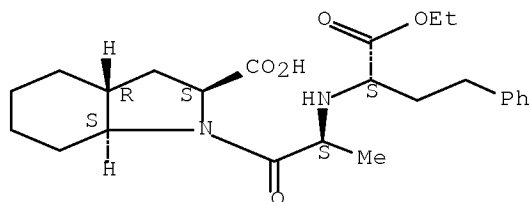
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-alanine derivs. with an ACE inhibitor effect)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 200423-23-0 CAPLUS

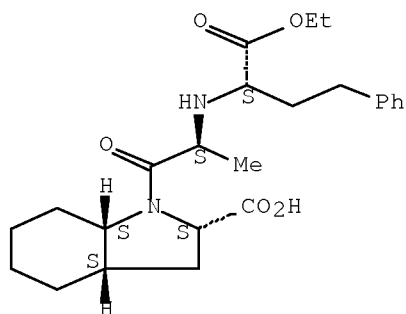
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3a $\beta$ , 7a $\beta$ ]]-, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 80876-01-3

CMF C24 H34 N2 O5

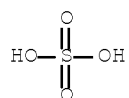
Absolute stereochemistry.



CM 2

CRN 7664-93-9

CMF H2 O4 S



IT 80876-01-3P

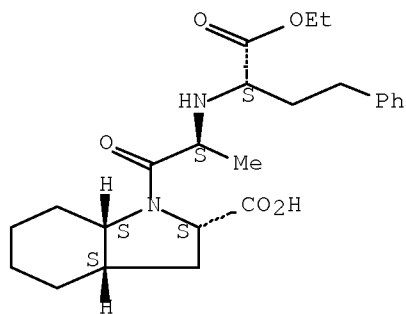
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-alanine derivs. with an ACE inhibitor effect)

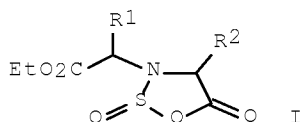
RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

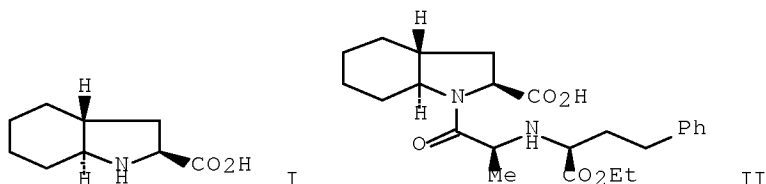


✓ L36 ANSWER 89 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of carboxylic α-N-sulfino cyclic anhydrides as ACE  
 inhibitor intermediates



## **L36 ANSWER 90 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

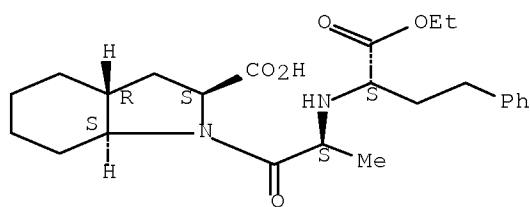
AN 1992:651183 CAPLUS [Full-text](#)  
 DN 117:251183  
 OREF 117:43483a, 43486a  
 TI Stereoselective synthesis of a trans-octahydroindole derivative, precursor  
 of Trandolapril (RU 44 570), an inhibitor of angiotensin converting enzyme  
 AU Brion, F.; Marie, C.; Mackiewicz, P.; Roul, J. M.; Buendia, J.  
 CS Roussel Uclaf, Romainville, 93230, Fr.  
 SO Tetrahedron Letters (1992), 33(34), 4889-92  
 CODEN: TELEAY; ISSN: 0040-4039  
 DT Journal  
 LA English  
 OS CASREACT 117:251183  
 GI



AB A stereoselective synthesis of the trans-octahydroindole-2-carboxylic acid I a  
 key intermediate in the elaboration of Trandolapril (RU 44 570) (II) was  
 achieved. The optically active starting material used was obtained from meso-  
 di-Me 1,2-cyclohexanedicarboxylate by an enzymic hydrolysis.  
 IT 87679-37-6P, Trandolapril  
 RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
 (stereoselective synthesis of)  
 RN 87679-37-6 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-  
 phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).





✓ L36 ANSWER 91 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation and formulation of [(mercaptoalkyl)carbamoyl]benzoates as analgesics and cardiovascular agents

✓ L36 ANSWER 92 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents

✓ L36 ANSWER 93 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of tripeptides with N terminal carbamoyl or acyl groups as renin inhibitors

✓ L36 ANSWER 94 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Preparation of carboxyalkyl dipeptides useful as angiotensin-converting enzyme (ACE) inhibitors

✓ 36 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI ✓ Ester prodrug derivatives of carboxylic acid drugs  
 AB Ester derivs.  $\text{RCO}_2(\text{CH}_2)_n\text{CONR}_1\text{R}_2$  [ $\text{RCO}_2$  = acyloxy residue of a carboxylic acid drug;  $\text{R}_1, \text{R}_2$  = (substituted) alkyl, alkenyl, aryl, aralkyl, or cycloalkyl, or  $\text{R}_1\text{NR}_2$  = (substituted) ring optionally containing addnl. N, O, or S;  $n = 1-3$ ] are prodrugs of carboxylic acid drugs  $\text{RCO}_2\text{H}$  which are highly stable in aqueous solution but highly susceptible to enzymic hydrolysis in vivo. They are less irritating to the mucosa than the parent drugs and may provide improved bioavailability. The plasma concentration of naproxen in rabbits reached a peak of  $7.4 \mu\text{g/mL}$  100 min after oral administration of naproxen ( $4.8 \text{ mg/kg}$ ), compared to a peak value of  $8.3 \mu\text{g/mL}$  50 min after oral administration of an equivalent amount of naproxen N,N-bis( $\beta$ -hydroxyethyl)glycolamide ester (I). The half-life for hydrolysis of I in 80% human plasma at  $37^\circ$  and pH 7.4 was 1.3 min. I was prepared by reaction of naproxen and  $\text{ClCH}_2\text{CON}(\text{CH}_2\text{CH}_2\text{OH})_2$ .

√ L36 ANSWER 96 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

√ TI Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation

√ AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]-β-alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mmHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mmHg with the ACE inhibitor alone.

## **L36 ANSWER 97 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1987:407555 CAPLUS [Full-text](#)

DN 107:7555

OREF 107:1399a,1402a

TI Synthesis and structure activity relationships of potent new angiotensin converting enzyme inhibitors containing saturated bicyclic amino acids

AU Blankley, C. J.; Kaltenbronn, J. S.; DeJohn, D. E.; Werner, A.; Bennett, L. R.; Bobowski, G.; Krolls, U.; Johnson, D. R.; Pearlman, W. M.

CS Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA

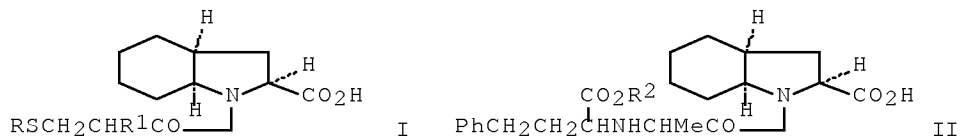
SO Journal of Medicinal Chemistry (1987), 30(6), 992-8  
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 107:7555

GI



AB The synthesis of a series of angiotensin-converting enzyme (ACE) inhibitors containing saturated bicyclic amino acids in place of proline is described. Octahydroindole-2-carboxylic acid, octahydroisoindole-1- carboxylic acid, and octahydro-3-oxoisindole-1-carboxylic acid can replace proline in both sulfhydryl and nonsulfhydryl compds.; e.g., sulfhydryl compds. I (R = Ac, H; R1 = H, Me) and nonsulfhydryl compds. II (R2 = Et, H) were prepared. Many of the compds. were equipotent to captopril and enalapril in both in vitro and in vivo ACE-inhibiting activity. Structure-activity relationships are discussed. Indolapril II (R2 = Et) has advanced to clin. evaluation.

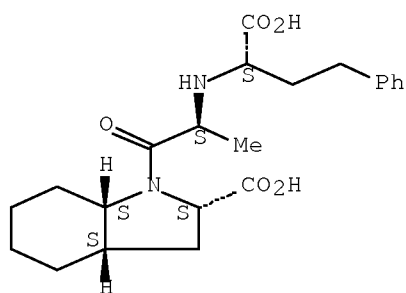
IT 80828-34-8P 80876-05-7P 80923-95-1P  
108449-50-9P 108449-51-0P 108449-52-1P  
108449-53-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and angiotensin converting enzyme-inhibiting activity of)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

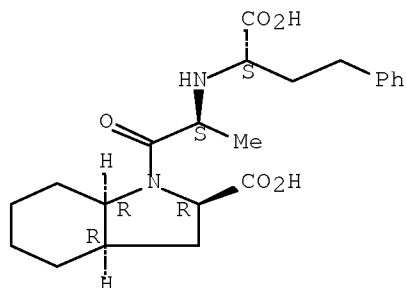
Absolute stereochemistry.



RN 80876-05-7 CAPLUS

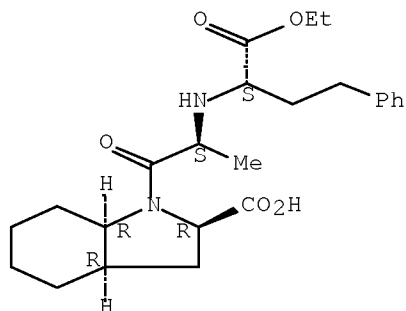
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(S\*)],2 $\alpha$ ,3a $\beta$ ,7a $\beta$ ]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



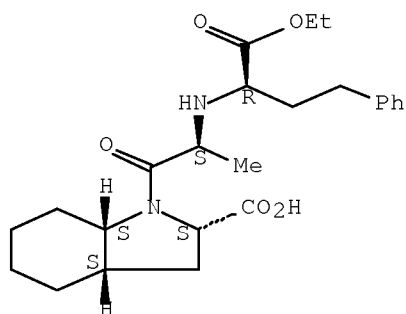
RN 80923-95-1 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(S\*)], 2 $\alpha$ , 3a $\beta$ , 7a $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



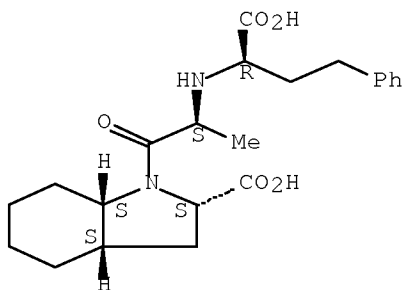
RN 108449-50-9 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(S\*)], 2 $\alpha$ , 3a $\beta$ , 7a $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 108449-51-0 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(S\*)], 2 $\alpha$ , 3a $\beta$ , 7a $\beta$ ]]- (9CI) (CA INDEX NAME)

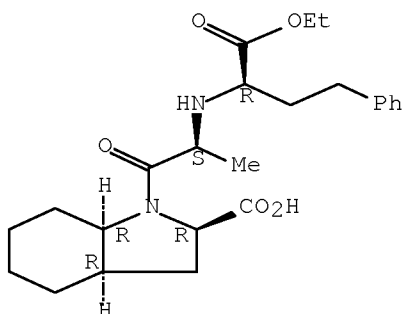
Absolute stereochemistry.



RN 108449-52-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[S\*(R\*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

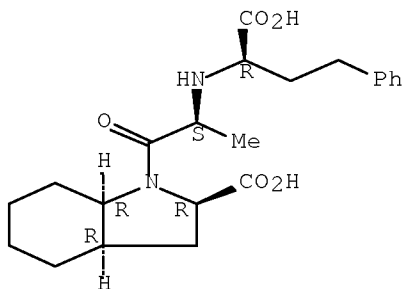


● HCl

RN 108449-53-2 CAPLUS

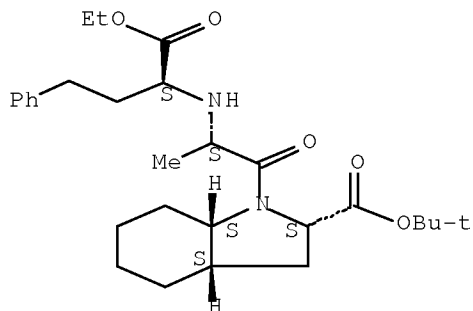
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(R\*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



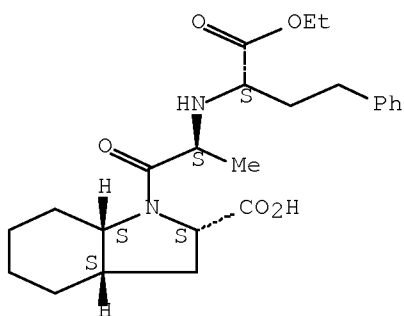
IT 80828-33-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrolysis of)  
 RN 80828-33-7 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha$  $\beta$ , 7 $\alpha$  $\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 80828-32-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and saponification and angiotensin converting enzyme-inhibiting activity of)  
 RN 80828-32-6 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1S]-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S,3 $\alpha$ S,7 $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry.

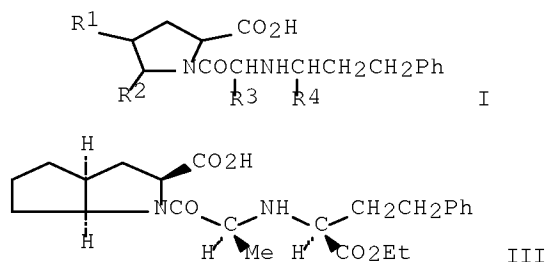


● HCl

## STN

AN 1987:85063 CAPLUS Full-text  
DN 106:85063  
OREF 106:13977a,13980a  
TI A new method of obtaining N-acylated proline derivatives  
IN Tremul Lozano, Jesus  
PA Lazlo Internacional S. A., Spain  
SO Span., 8 pp.  
CODEN: SPXXAD  
DT Patent  
LA Spanish  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	ES 549789	A1	19860316	ES 1985-549789	19851210
PRAI	ES 1985-549789		19851210		
GI					

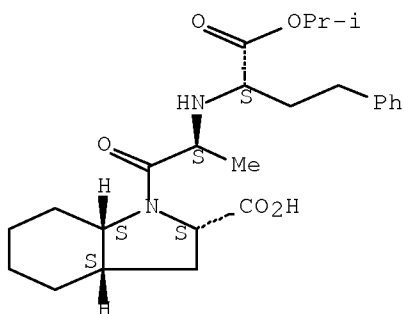


AB Title derivs. I [R1, R2 = H, alkyl; R1R2 = (CH2)n; n = 3, 4; R3 = alkyl, (CH2)mNH2; m = 3, 4; R4 = OH, alkoxy] are prepared by reacting the corresponding acids (NH2-protected as needed) with 1-(2-nitrophenylsulfonyloxy)-6-nitrobenzotriazole (II) in the presence of a base, followed by treatment of the resulting intermediates in situ with the corresponding CO2H-protected amino acids and addnl. base, and final deprotection. Thus, a mixture of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-(S)-alanine, II, and Et3N in MeCN was stirred and treated with a solution of benzyl cis-octahydrocyclopenta[b]pyrrole-2(S)-carboxylate and Et3N in MeCN, followed by workup involving catalytic hydrogenation, to give peptide derivative III.

IT 106554-58-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, by peptide coupling with benzotriazolyl sulfonate derivative)

RN 106554-58-9 CAPLUS  
CN 1H-Indole-2-carboxylic acid, octahydro-1-[2-[[1-[(1-methylethoxy)carbonyl]-3-phenylpropyl]amino]-1-oxopropyl]-, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha$ , 7 $\alpha$ .b eta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## **L36 ANSWER 99 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1987:67669 CAPLUS [Full-text](#)

DN 106:67669

OREF 106:11147a,11150a

TI Indolapril

IN Linan Castellet, Isidro; Oliver Mir, Monica

PA Farmhispania S. A., Spain; Bioiberica S. A.

SO Span., 13 pp.

CODEN: SPXXAD

DT Patent

LA Spanish

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	ES 537841	A1	19860116	ES 1984-537841	19841121
PRAI	ES 1984-537841		19841121		

AB The title compound, useful as an antihypertensive (no data), was prepared An indole-2-carboxylic acid derivative was N-acylated by MeCHBrCOBr and NaHCO<sub>3</sub> and the product was treated with (S)-PhCH<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>Et and Et<sub>3</sub>N to give Indolapril.

IT 80876-01-3F, Indolapril

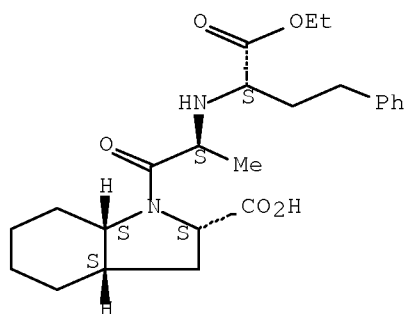
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of, as antihypertensive)

RN 80876-01-3 CAPLUS

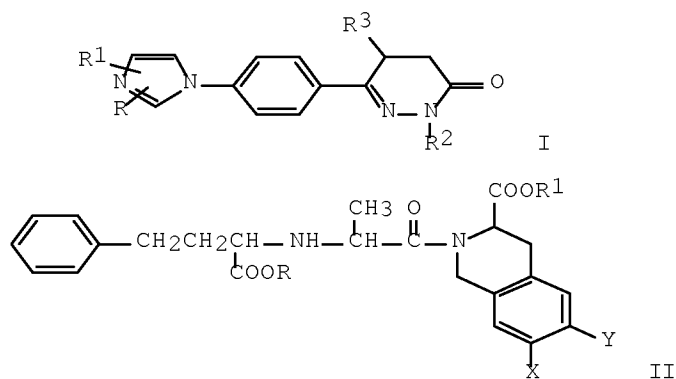
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.





√ L36 ANSWER 100 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI √ Medicaments and method of treating heart failure



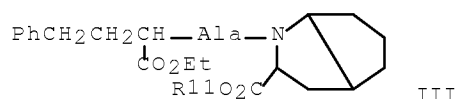
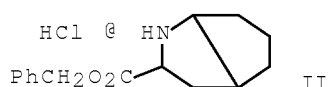
√ L36 ANSWER 101 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 √ TI Treatment of coronary insufficiency  
 IN Henning, Rainer; Urbach, Hansjoerg; Teetz, Volker; Geiger, Rolf;  
 Schoelkens, Bernward

## **L36 ANSWER 102 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1985:560859 CAPLUS Full-text  
 DN 103:160859  
 OREF 103:25849a,25852a  
 TI N-Alkylated dipeptides and their esters  
 IN Teetz, Volker; Wissmann, Hans; Urbach, Hansjoerg  
 PA Hoechst A.-G. , Fed. Rep. Ger.  
 SO Eur. Pat. Appl., 33 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA German  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 135182	A2	19850327	EP 1984-110678	19840907
	EP 135182	A3	19860305		
	EP 135182	B1	19880727		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	DE 3333454	A1	19850411	DE 1983-3333454	19830916
	AT 35997	T	19880815	AT 1984-110678	19840907
	HU 36145	A2	19850828	HU 1984-3415	19840910
	HU 201565	B	19901128		
	FI 8403590	A	19850317	FI 1984-3590	19840913
	FI 80464	B	19900228		
	FI 80464	C	19900611		
	CA 1338163	C	19960312	CA 1984-463078	19840913
	DK 8404405	A	19850317	DK 1984-4405	19840914
	DK 164939	B	19920914		
	DK 164939	C	19930201		
	NO 8403662	A	19850318	NO 1984-3662	19840914
	NO 167743	B	19910826		
	NO 167743	C	19911204		
	AU 8433070	A	19850321	AU 1984-33070	19840914
	AU 576782	B2	19880908		
	JP 60089497	A	19850520	JP 1984-191868	19840914
	JP 07098835	B	19951025		
	ZA 8407257	A	19850529	ZA 1984-7257	19840914
	ES 535917	A1	19851001	ES 1984-535917	19840914
	IL 72947	A	19890228	IL 1984-72947	19840914
	US 5068351	A	19911126	US 1990-560004	19900727
PRAI	DE 1983-3333454	A	19830916		
	EP 1984-110678	A	19840907		
	US 1984-650715	B1	19840914		
	US 1986-943882	B1	19861219		
	US 1988-178767	B1	19880330		
	US 1989-403919	B1	19890907		
OS	MARPAT 103:160859				
GI					



AB Title compds. R3O2CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue]; R1 = H, (un)usbsituted C1-6 aliphatic, C3-9 alicyclic, C4-13 alicyclic aliphatic, C6-12 aromatic, C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un)substituted C1-6 aliphatic, C3-9 alicyclic, C6-12 aromatic, or C7-16 araliph. residue; CHR4NR5 = C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of HO2CCHR1NHCH(CO2R2)(CH2)nR with R3O2CCHR4NHR5 in the presence of phosphinic acid anhydrides R7R8P(O)OP(O)R9R10 (R7, R8, R9, R10 = alkyl or aralkyl). Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH by ethylmethylphosphinic acid anhydride in CH2Cl2 containing Et3N to give peptide III (R11 = CH2Rh), which was debenzylated to give III (R1 = H). I

inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

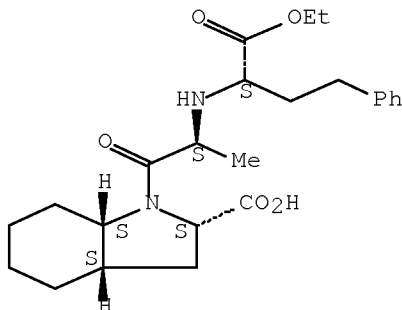
IT 80828-32-6P 83542-05-6P 98677-37-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

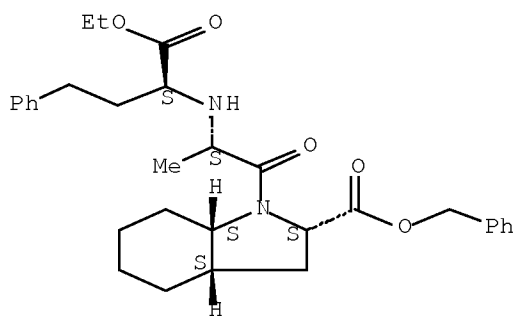


● HCl

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI) (CA INDEX NAME)

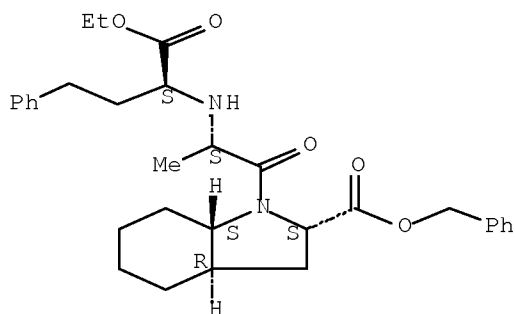
Absolute stereochemistry.



RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



## **L36 ANSWER 103 OF 111 CAPLUS COPYRIGHT 2008 ACS**

### **on STN**

AN 1985:560858 CAPLUS [Full-text](#)

DN 103:160858

OREF 103:25849a,25852a

TI N-Alkylated dipeptides and their esters

IN Urbach, Hansjoerg; Henning, Rainer; Wissmann, Hans; Teetz, Volker

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 32 pp.

CODEN: EPXXDW

DT Patent

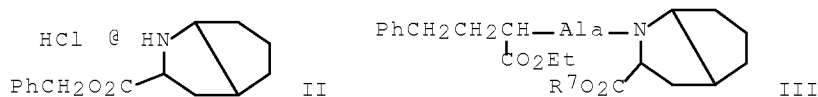
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 135181	A2	19850327	EP 1984-110677	19840907
	EP 135181	A3	19860402		
	EP 135181	B1	19900131		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	DE 3333455	A1	19850411	DE 1983-3333455	19830916
	AT 49979	T	19900215	AT 1984-110677	19840907
	HU 36140	A2	19850828	HU 1984-3417	19840910
	HU 198303	B	19890928		
	FI 8403591	A	19850317	FI 1984-3591	19840913
	FI 80275	B	19900131		
	FI 80275	C	19900510		
	CA 1338162	C	19960312	CA 1984-463071	19840913
	DK 8404404	A	19850317	DK 1984-4404	19840914
	DK 166027	B	19930301		
	DK 166027	C	19930712		
	NO 8403663	A	19850318	NO 1984-3663	19840914
	NO 167808	B	19910902		
	NO 167808	C	19911218		
	AU 8433071	A	19850321	AU 1984-33071	19840914
	AU 575585	B2	19880804		
	JP 60089498	A	19850520	JP 1984-191869	19840914
	JP 07098836	B	19951025		
	ZA 8407259	A	19850529	ZA 1984-7259	19840914
	ES 535918	A1	19851001	ES 1984-535918	19840914
	IL 72946	A	19900429	IL 1984-72946	19840914
	US 5055591	A	19911008	US 1988-173024	19880323
PRAI	DE 1983-3333455	A	19830916		
	EP 1984-110677	A	19840907		

US 1984-650714                      B1        19840914  
 US 1986-943881                      B1        19861219

GI



AB Title compds.  $\text{R}_3\text{O}_2\text{CCHR}_4\text{NR}_5\text{COCHR}_1\text{NHCH}(\text{CO}_2\text{R}_2)(\text{CH}_2)_n\text{R}$  [I;  $n = 1, 2$ ;  $\text{R} = \text{H}$ , (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [ $\text{R}_6 =$  (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue];  $\text{R}_1 = \text{H}$ , (un)substituted C3-9 alicyclic, C4-13 alicyclic aliphatic, C6-12 aromatic, C7-16 araliph., or heteroarom. residue, amino acid side chain;  $\text{R}_2, \text{R}_3 = \text{H}$ , (un)substituted C1-6 aliphatic, C3-9 alicyclic, C6-12 aromatic, or C7-16 araliph. residue;  $\text{CHR}_4\text{NR}_5 =$  C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of  $\text{HO}_2\text{CCHR}_1\text{NHCH}(\text{CO}_2\text{R}_2)(\text{CH}_2)_n\text{R}$  with  $\text{R}_3\text{O}_2\text{CCHR}_4\text{NR}_5$  in the presence of an alkanephosphoric acid anhydride. Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)- $\text{PhCH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{Et})-\text{Ala}-\text{OH}$  by n-propanephosphonic acid anhydride in  $\text{CH}_2\text{Cl}_2$  in the presence of N-ethylmorpholine to give peptide derivative III ( $\text{R}_7 = \text{CH}_2\text{Ph}$ ), which was debenzylated to give III ( $\text{R}_7 = \text{H}$ ) (all-S isomer). I inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

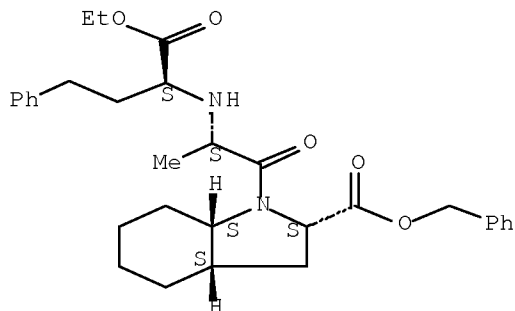
IT 83542-05-6P 98677-37-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha$ , 7 $\alpha$ ]]- (9CI) (CA INDEX NAME)

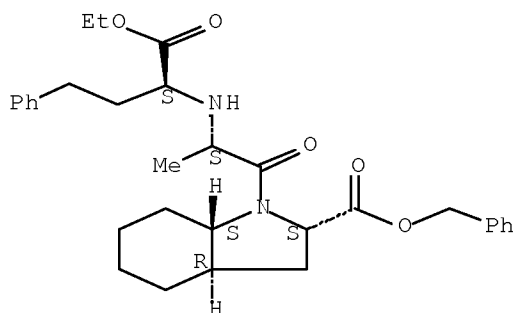
Absolute stereochemistry.



RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3 $\alpha$ R, 7 $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry.



## **L36 ANSWER 104 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1985:185278 CAPLUS Full-text

DN 102:185278

OREF 102:29073a,29076a

TI Phosphate salts of 1-(2-[(1-alkoxycarbonyl-3-aralkyl)amino]-1-oxoalkyl)octahydro-1H-indole-2-carboxylic acids

IN Seamans, Ronald E.; Behnke, Walter E.

PA Warner-Lambert Co. , USA

SO U.S., 5 pp.

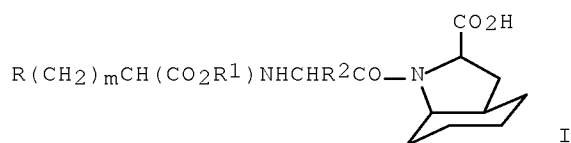
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4490386	A	19841225	US 1982-422499	19820923
PRAI	US 1982-422499		19820923		
OS	CASREACT 102:185278; MARPAT 102:185278				
GI					



AB One example of a phosphate salt of acylated octahydroindolecarboxylic acids I [R = (un)substituted Ph; m = 0-3; R1 = H, alkyl; R2 = H, alkyl, PhCH2], antihypertensives (no data) was prepared Thus, the S,S-isomer of Et  $\alpha$ -[(1-carboxyethyl)amino]benzenebutanoate hydrochloride was treated with tert-Bu (1)-octahydro-1H-indole-2-carboxylate in the presence of 1-hydroxytriazole, Et3N, and dicyclohexylcarbodiimide to give the S,S,S-isomer of I (R = Ph, m = 2, R1 = Et, R2 = Me) as the HCl salt (II). Treating II with 85% H3PO4 gave the 1:1 phosphate salt.

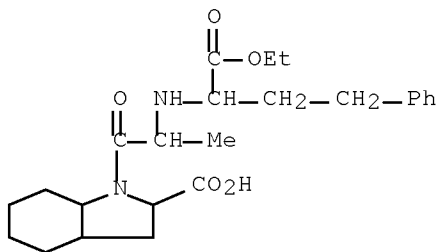
IT 96022-35-4F

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and formation of phosphate salt from)

RN 96022-35-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT 96015-97-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

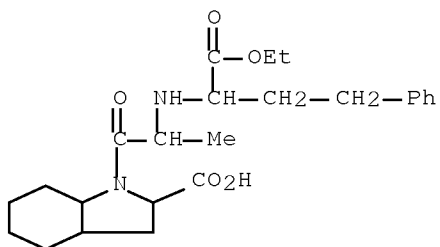
RN 96015-97-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 80876-02-4

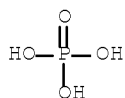
CMF C24 H34 N2 O5



CM 2

CRN 7664-38-2

CMF H3 O4 P



## **L36 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2008 ACS**

### **on STN**

AN 1984:139616 CAPLUS Full-text

DN 100:139616

OREF 100:21335a,21338a

TI Derivatives of bicyclic amino acids, agents containing them and their use, as well as bicyclic amino acids as intermediates

IN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard; Gaul, Holger

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 103 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 84164	A2	19830727	EP 1982-112007	19821224
	EP 84164	A3	19831012		
	EP 84164	B1	19870128		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	DE 3151690	A1	19830707	DE 1981-3151690	19811229
	DE 3210701	A1	19831006	DE 1982-3210701	19820324
	EP 170775	A1	19860212	EP 1985-103730	19821224
	EP 170775	B1	19891108		
	EP 170775	B2	19941012		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 25244	T	19870215	AT 1982-112007	19821224
PRAI	DE 1981-3151690	A	19811229		
	DE 1982-3210701	A	19820324		
	EP 1982-112007	P	19821224		

OS CASREACT 100:139616

GI For diagram(s), see printed CA Issue.

AB Title compds. I [R = H, C1-6 alkyl, aminoalkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, C5-7 cycloalkyl-C1-4 alkyl, (un)substituted aryl or partially hydrogenated aryl; R1 = H, C1-6 alkyl, C2-6 alkenyl, aryl-C1-4 alkyl; R2 = H, OH; R3 = H; R2R3 = O; R4 = C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, (un)substituted aryl, indol-3-yl; n = 0, 1, 2] were prepared as antihypertensives due to their ability to inhibit angiotensin-converting enzyme (ACE). Thus, (S)-PhCH2CH2CH(CO2Et)-(S)-Ala- OH was condensed with (d,l)-2 $\beta$ ,3a $\beta$ ,7a $\beta$ -octahydroindole-3- carboxylic acid benzyl ester-HCl by DCC/1-hydroxybenzotriazole in DMF containing N-ethylmorpholine to give a mixture of the (2S,3aR,7aR)- and (2R,3aS,7aS)-diastereoisomers of octahydroindole II (R5 = Et, R6 = CH2Ph) (III). (2S,3aR,7aR)-III was debenzylated by hydrogenolysis and then saponified to give (2S,3aR,7aR)-II (R5 = R6 = H). (2S,3aR,7aS)-II (R5 = R6 = H) inhibited ACE in rats with an ED50 of 800  $\mu$ g/kg.

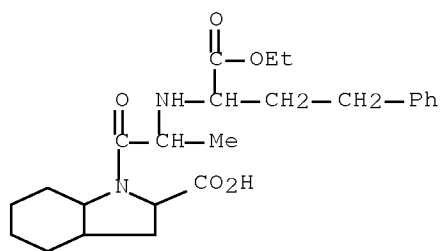
IT 80876-02-4 83601-86-9

RL: RCT (Reactant); RACT (Reactant or reagent)

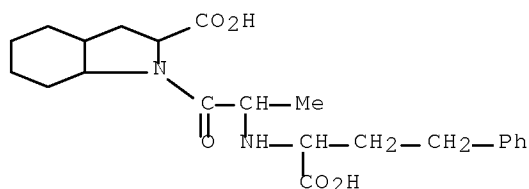
(angiotensin converting enzyme-inhibiting activity of)



RN 80876-02-4 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

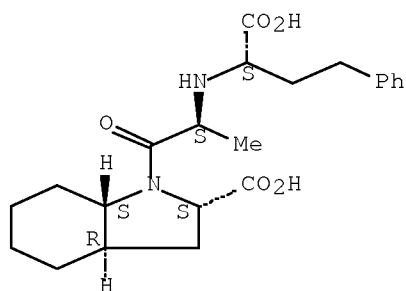


RN 83601-86-9 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



IT 87679-71-8P 87679-72-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation and angiotensin converting enzyme-inhibiting activity of)  
 RN 87679-71-8 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

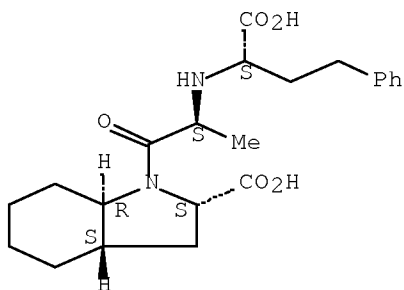
Absolute stereochemistry.



RN 87679-72-9 CAPLUS

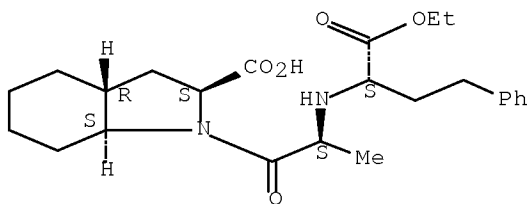
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3a $\beta$ ,7a $\alpha$ ]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



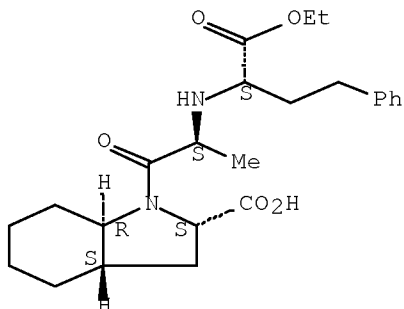
IT 87679-37-6P 87679-42-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and angiotensin-converting enzyme-inhibiting activity of)  
RN 87679-37-6 CAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 87679-42-3 CAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3a $\beta$ ,7a $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



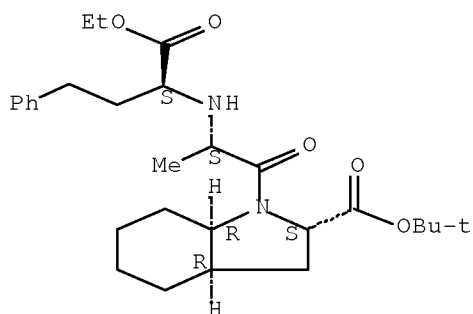
IT 87679-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and de-tert-butylation of)

RN 87679-29-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha\alpha$ , 7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



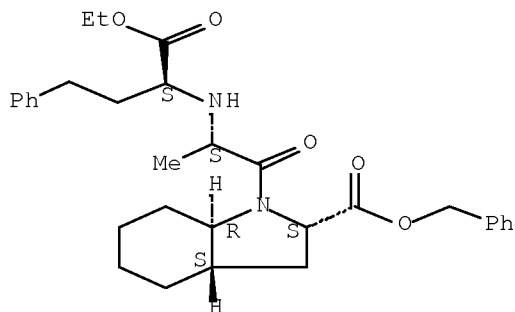
IT 87679-41-2P 87827-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and hydrogenolysis of)

RN 87679-41-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3 $\alpha$ S, 7 $\alpha$ R)- (CA INDEX NAME)

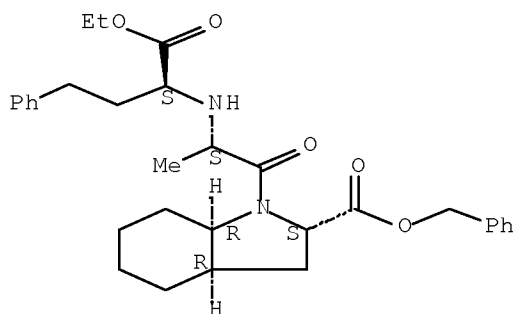
Absolute stereochemistry.



RN 87827-53-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha\alpha$ , 7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



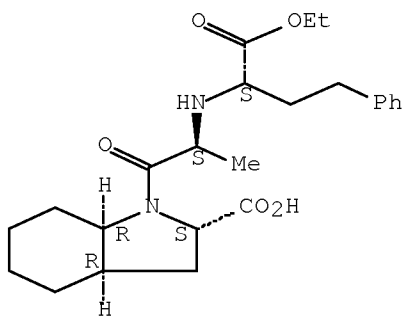
IT 87725-71-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)

RN 87725-71-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[R\*(R\*)], 2α, 3α, 7α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

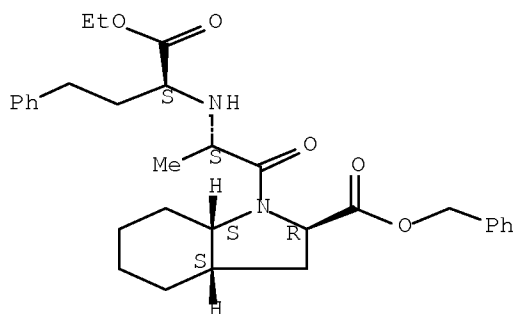
IT 87679-28-5P 87679-32-1P 87679-40-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 87679-28-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2R-[1[S\*(S\*)], 2α, 3α, 7α]]- (9CI) (CA INDEX NAME)

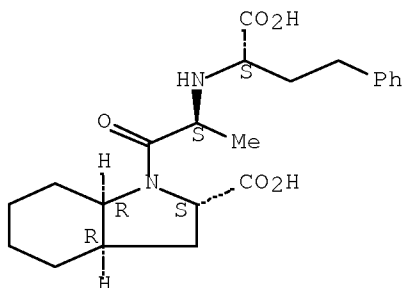
Absolute stereochemistry.



RN 87679-32-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)], 2α, 3αα, 7αα]]- (9CI)  
(CA INDEX NAME)

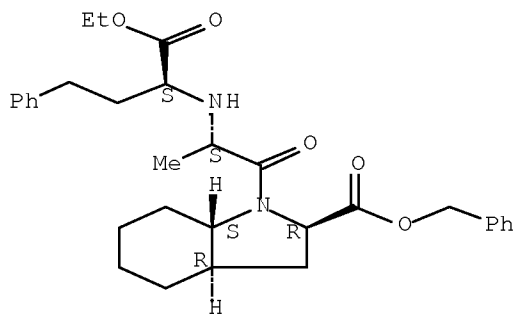
Absolute stereochemistry.



RN 87679-40-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2R, 3aR, 7aS)- (CA INDEX NAME)

Absolute stereochemistry.



**L36 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2008 ACS****on STN**AN 1984:34404 CAPLUS Full-text

DN 100:34404

OREF 100:5335a,5338a

TI Derivatives of bicyclic amino acids, an agent containing them, their use, and bicyclic amino acids as intermediates

IN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Ger. Offen., 79 pp.

CODEN: GWXXBX

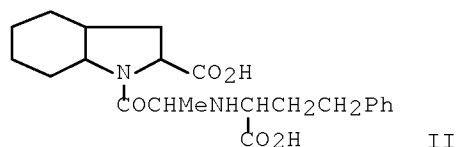
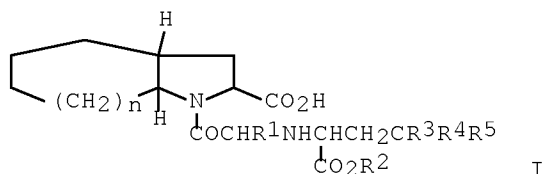
DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	DE 3151690	A1	19830707	DE 1981-3151690	19811229
	CA 1341296	C	20010925	CA 1982-418453	19821223
	AU 8291931	A	19830707	AU 1982-91931	19821224
	AU 559140	B2	19870226		
	EP 84164	A2	19830727	EP 1982-112007	19821224
	EP 84164	A3	19831012		
	EP 84164	B1	19870128		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 170775	A1	19860212	EP 1985-103730	19821224
	EP 170775	B1	19891108		
	EP 170775	B2	19941012		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 25244	T	19870215	AT 1982-112007	19821224
	AT 47838	T	19891115	AT 1985-103730	19821224
	FI 8204474	A	19830630	FI 1982-4474	19821227
	FI 80017	B	19891229		
	FI 80017	C	19900410		
	JP 58118569	A	19830714	JP 1982-227179	19821227
	JP 05087504	B	19931216		
	ES 518574	A1	19831001	ES 1982-518574	19821227
	IL 67572	A	19920818	IL 1982-67572	19821227
	DK 8205767	A	19830630	DK 1982-5767	19821228
	DK 170444	B1	19950904		
	NO 8204394	A	19830630	NO 1982-4394	19821228
	NO 156786	B	19870817		
	NO 156786	C	19871125		
	ZA 8209523	A	19831026	ZA 1982-9523	19821228
	HU 27438	A2	19831028	HU 1982-4177	19821228
	HU 194278	B	19880128		
	HU 194167	B	19880128	HU 1984-4653	19821228
	ES 521740	A1	19840116	ES 1983-521740	19830422
	NO 8302741	A	19830630	NO 1983-2741	19830727
	NO 158799	B	19880725		
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	CA 1206478	A2	19860624	CA 1984-461836	19840824
	US 5008400	A	19910416	US 1984-673605	19841121
	FI 8803456	A	19880721	FI 1988-3456	19880721
	FI 80675	B	19900330		
	FI 80675	C	19900710		
	JP 01301695	A	19891205	JP 1989-7870	19890118
	JP 01301659	A	19891205	JP 1989-7871	19890118
	JP 06004586	B	19940119		

	US 4933361	A	19900612	US 1989-346339	19890428
	US 5101039	A	19920331	US 1990-468567	19900123
	DK 9201199	A	19920928	DK 1992-1199	19920928
	DK 171232	B1	19960805		
PRAI	DE 1981-3151690	A	19811229		
	DE 1982-3210701	A	19820324		
	CA 1982-418453	A3	19821223		
	EP 1982-112007	P	19821224		
	EP 1985-103730	A	19821224		
	FI 1982-4474	A	19821227		
	US 1982-453092	B3	19821227		
	US 1984-673605	A1	19841121		
OS	MARPAT 100:34404				
GI					



AB Pyrrolecaryoxylic acids I [n = 0-2; R1 = H, alkyl (un)substituted by amino, cycloalkyl, or aryl, (un)substituted alkenyl, cycloalk(en)yl, or (partly hydrogenated)aryl, cyclo- or bicyclic heterocyclyl, side-chain of a naturally occurring amino acid; R2 = H, alk(en)yl, arylalkyl; R3 = alk(en)yl, cycloalkyl, (un)substituted aryl; R4 = H, OH; R5 = H, R4R5 = O] and their physiol. tolerable salts, useful as antihypertensives (ED50 40-1080 µg/kg in rats), were prepared N-[1-(S)-Carboxy-3-phenylpropyl]- (S)-alanyl- (2S,3aR,7aR)octahydroindole-2-carboxylic acid II was prepared in 9 steps from indole.

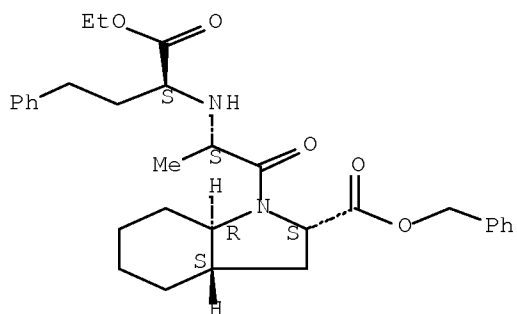
IT 87679-41-2P 87827-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and debenzilation of)

RN 87679-41-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aR)- (CA INDEX NAME)

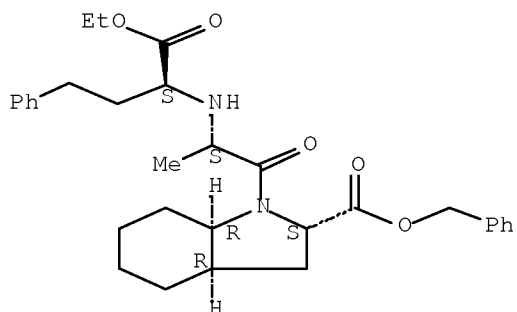
Absolute stereochemistry.



RN 87827-53-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(R\*)], 2α, 3αα, 7αα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



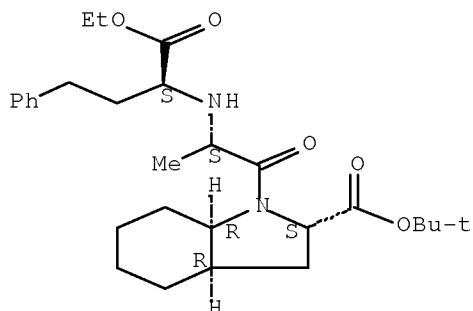
IT 87679-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 87679-29-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R\*(R\*)], 2α, 3αα, 7αα]]- (9CI) (CA INDEX NAME)

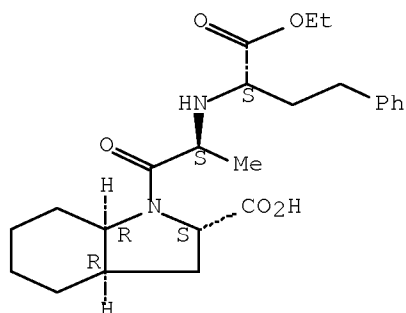
Absolute stereochemistry.





IT 87725-71-1P 87725-72-2P 87725-73-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and saponification of)  
 RN 87725-71-1 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-  
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,  
 [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha\alpha$ , 7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

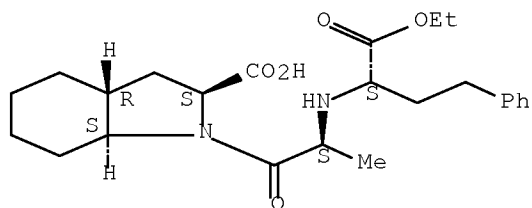
Absolute stereochemistry.



● HCl

RN 87725-72-2 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(ethoxycarbonyl)-3-  
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,  
 (2S, 3 $\alpha$ R, 7 $\alpha$ S)- (9CI) (CA INDEX NAME)

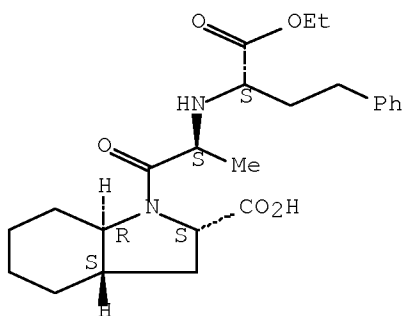
Absolute stereochemistry. Rotation (-).



● HCl

RN 87725-73-3 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-  
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,  
 [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha\beta$ , 7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

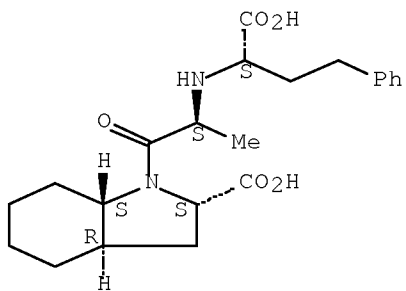
IT ~~87679-71-8~~ 87679-72-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation as antihypertensive)

RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

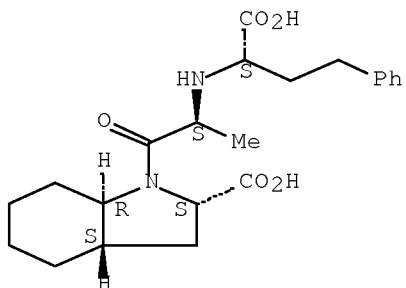
Absolute stereochemistry.



RN 87679-72-9 CAPLUS

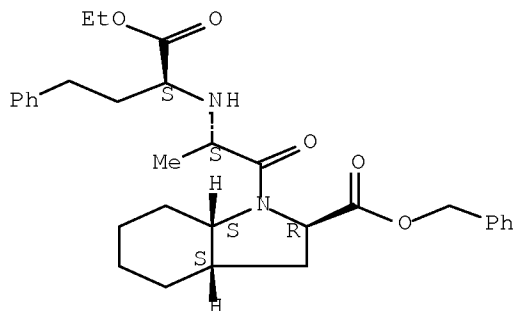
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3a $\beta$ ,7a $\alpha$ ]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



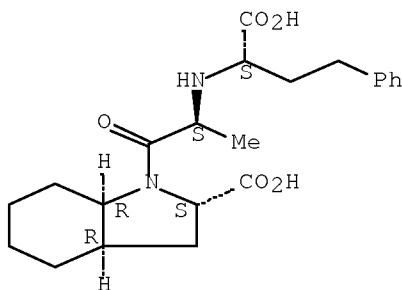
IT 87679-28-5P 87679-32-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 87679-28-5 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2R-[1[S\*(S\*)],2 $\alpha$ ,3 $\alpha\alpha$ ,7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 87679-32-1 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha\alpha$ ,7 $\alpha\alpha$ ]]- (9CI)  
 (CA INDEX NAME)

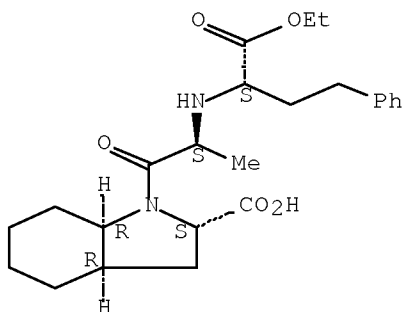
Absolute stereochemistry.



IT 87679-36-5P 87679-37-6P 87679-40-1P  
 87679-42-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as antihypertensive)  
 RN 87679-36-5 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-

[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha\alpha$ ,7 $\alpha\alpha$ ]]- (9CI) (CA INDEX NAME)

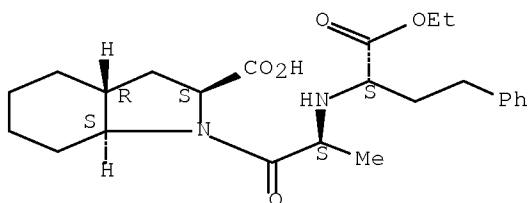
Absolute stereochemistry.



RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3 $\alpha$ R,7 $\alpha$ S)- (CA INDEX NAME)

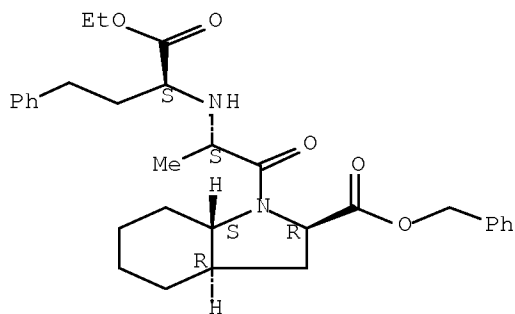
Absolute stereochemistry. Rotation (-).



RN 87679-40-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2R,3 $\alpha$ R,7 $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry.

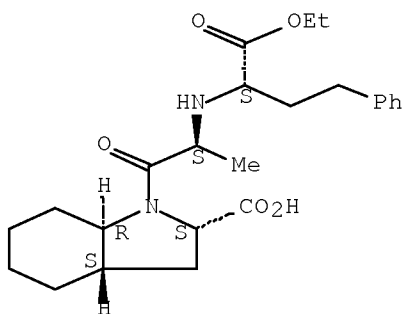


RN 87679-42-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-  
[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha$ , 7 $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

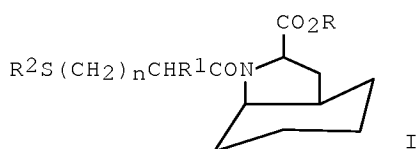


## **L36 ANSWER 107 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1983:143272 CAPLUS Full-text  
DN 98:143272  
OREF 98:21821a,21824a  
TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids  
IN Hoefle, Milton L.; Bobowski, George  
PA Warner-Lambert Co. , USA  
SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 194,307, abandoned.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 4350704	A	19820921	US 1981-233940	19810217
	IL 62294	A	19860731	IL 1981-62294	19810304
	IL 71045	A	19860731	IL 1981-71045	19810304
	ZA 8101493	A	19820331	ZA 1981-1493	19810305
	CA 1205476	A1	19860603	CA 1981-372381	19810305
	EP 37231	A2	19811007	EP 1981-301243	19810324
	EP 37231	A3	19820428		
	EP 37231	B1	19870128		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	EP 88341	A1	19830914	EP 1983-101990	19810324
	EP 88341	B1	19870722		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 88342	A1	19830914	EP 1983-101991	19810324
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 25243	T	19870215	AT 1981-301243	19810324
	AT 28452	T	19870815	AT 1983-101990	19810324
	FI 8100971	A	19811003	FI 1981-971	19810330
	FI 76072	B	19880531		
	FI 76072	C	19880909		
	AU 8168939	A	19811008	AU 1981-68939	19810331
	AU 543861	B2	19850509		
	DK 8101482	A	19811003	DK 1981-1482	19810401
	DK 157851	B	19900226		

DK 157851	C	19900730		
NO 8101121	A	19811005	NO 1981-1121	19810401
NO 156609	B	19870713		
NO 156609	C	19871021		
ES 500965	A1	19820816	ES 1981-500965	19810401
HU 25950	A2	19830829	HU 1981-846	19810401
HU 183383	B	19840428		
HU 30000	A2	19840228	HU 1983-1049	19810401
HU 187880	B	19860228		
JP 56161372	A	19811211	JP 1981-48512	19810402
JP 02047480	B	19901019		
US 4425355	A	19840110	US 1981-277794	19810629
ES 504189	A1	19820616	ES 1981-504189	19810722
DD 201782	A5	19830810	DD 1981-233893	19811005
DD 202146	A5	19830831	DD 1981-233892	19811005
SU 1246893	A3	19860723	SU 1981-3339202	19811005
SU 1241988	A3	19860630	SU 1982-3498497	19821010
FI 8504743	A	19851129	FI 1985-4743	19851129
FI 76560	B	19880729		
FI 76560	C	19881110		
NO 8600366	A	19811005	NO 1986-366	19860203
NO 156898	B	19870907		
NO 156898	C	19871216		
DK 8800910	A	19880222	DK 1988-910	19880222
DK 159419	B	19901015		
DK 159419	C	19910318		
PRAI US 1980-137106	A2	19800402		
US 1980-194307	A2	19801006		
US 1981-233940	A	19810217		
EP 1981-301243	P	19810324		
EP 1983-101990	A	19810324		
FI 1981-971	A	19810330		
IL 1984-62294	A	19840531		
OS CASREACT 98:143272				
GI				



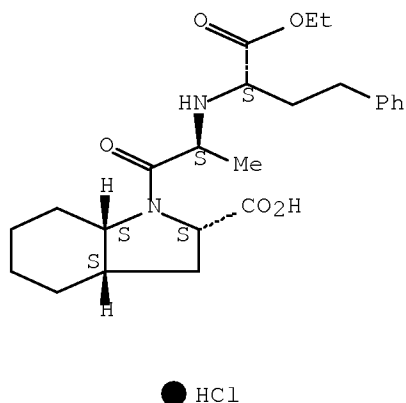
AB The antihypertensive title compds. I [R = H, alkyl; R1 = H, alkyl, PhCH2; R2 = H, R3CO (R3 = alkyl, (un)substituted phenyl); and their pharmaceutically acceptable salts; n = 0, 1] were prepared Thus, (+)-Et (2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ )-octahydro-1H-indole-2-carboxylate, prepared by hydrogenation of Et indole-2-carboxylate, was treated with AcSCH2CH2COCl to give Et (2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ )-octahydro-1-[3-(acetylthio)propanoyl]-1H-indole-2-carboxylate (II). The angiotensin converting enzyme inhibitory IC50 of II was 3.8 + 106 M.

IT 80828-32-6F 80828-34-8P 80876-03-5F  
 80876-05-7F  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and angiotensin converting enzyme inhibition by)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

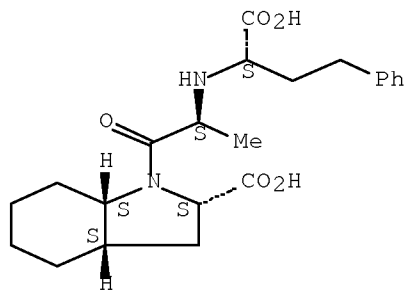
Absolute stereochemistry.



RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

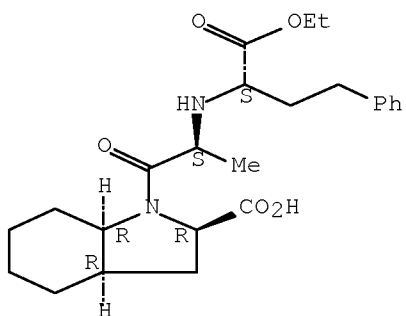
Absolute stereochemistry.



RN 80876-03-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[S\*(S\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

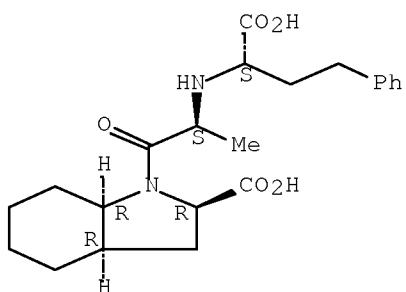


● HCl

RN 80876-05-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(S\*)], 2α, 3aβ, 7aβ]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IT 80828-33-7P

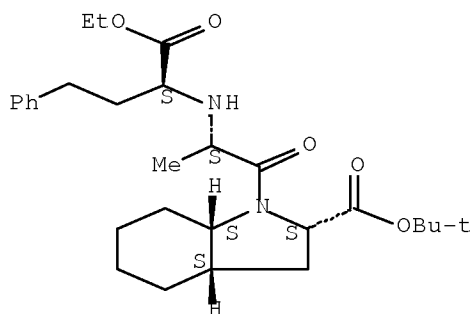
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and hydrolysis of)

RN 80828-33-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R\*(R\*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





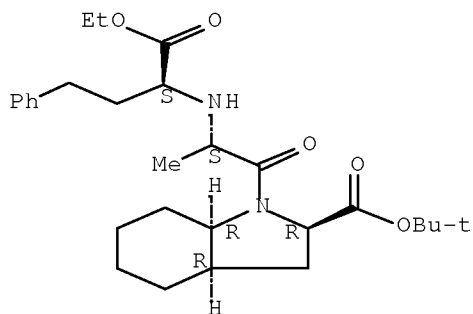
IT 80876-04-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and partial hydrolysis of)

RN 80876-04-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2R-[1[S\*(S\*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## **L36 ANSWER 108 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN**

AN 1982:616730 CAPLUS Full-text

DN 97:216730

OREF 97:36397a,36400a

TI Carboxyalkyl dipeptides and pharmaceutical compositions containing them

IN Neustadt, Bernard R.; Gold, Elijah H.; Smith, Elizabeth M.

PA Schering Corp., USA

SO Eur. Pat. Appl., 123 pp.

CODEN: EPXXDW

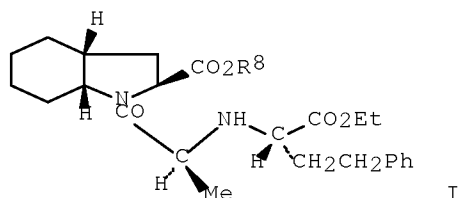
DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 50800	A1	19820505	EP 1981-108348	19811015
	EP 50800	B1	19860618		

EP 50800	B2	19950607		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 20469	T	19860715	AT 1981-108348	19811015
DK 8104625	A	19820424	DK 1981-4625	19811020
DK 161523	B	19910715		
DK 161523	C	19911223		
FI 8103283	A	19820424	FI 1981-3283	19811020
FI 83222	B	19910228		
FI 83222	C	19910610		
AU 8176614	A	19820429	AU 1981-76614	19811020
AU 554362	B2	19860821		
ZA 8107261	A	19820929	ZA 1981-7261	19811020
CA 1341206	C	20010320	CA 1981-388336	19811020
NO 8103546	A	19820426	NO 1981-3546	19811021
NO 164983	B	19900827		
NO 164983	C	19901205		
JP 57112359	A	19820713	JP 1981-168511	19811021
JP 01032240	B	19890629		
IL 64085	A	19861231	IL 1981-64085	19811021
HU 32785	A2	19840928	HU 1981-3078	19811022
HU 193146	B	19870828		
US 4587258	A	19860506	US 1984-635390	19840730
US 4808573	A	19890228	US 1987-29293	19870323
US 4818749	A	19890404	US 1987-117008	19871104
US 4831157	A	19890516	US 1988-250300	19880928
JP 01163197	A	19890627	JP 1988-283542	19881109
PRAI US 1980-199886	A	19801023		
US 1981-258484	A	19810428		
US 1980-201649	A2	19801028		
EP 1981-108348	A	19811015		
US 1981-334053	A2	19811223		
US 1984-635390	A2	19840730		
WO 1985-US1406	A	19850726		
US 1986-817639	A3	19860110		
US 1987-29293	A2	19870323		
OS MARPAT 97:216730				
GI				



AB RCOCR<sub>1</sub>R<sub>2</sub>NHCHR<sub>3</sub>CONR<sub>4</sub>CR<sub>5</sub>R<sub>7</sub>COR<sub>6</sub> [R, R<sub>6</sub> = OH, (un)substituted alkoxy, alkenyloxy, (un)substituted NH<sub>2</sub>; R<sub>1</sub> = H, (un)substituted alkyl; R<sub>2</sub>, R<sub>7</sub> = H, (un)substituted alkyl; R<sub>3</sub> = H, (un)substituted alkyl, (un)substituted phenylalkyl; R<sub>4</sub>, R<sub>5</sub> = H, (un)substituted alkyl; R<sub>4</sub>R<sub>5</sub> form ring systems] were prepared as antihypertensives and angiotensin-converting enzyme inhibitors (no data). Thus, H-L-Ala-OCH<sub>2</sub>Ph tosylate was treated with PhCH<sub>2</sub>CH<sub>2</sub>COC<sub>2</sub>Et and reduced with NaBH<sub>3</sub>(CN) and then debenzylated by hydrogenolysis to give (S)-PhCH<sub>2</sub>CH<sub>2</sub>CH(CO<sub>2</sub>Et)-L-Ala-OH. The latter was condensed with cis,syn-

octahydroindole-2(S)-carboxylic acid benzyl ester to give indole I (R8 = CH2Ph), which was debenzylated by hydrogenolysis to give I (R8 = H).

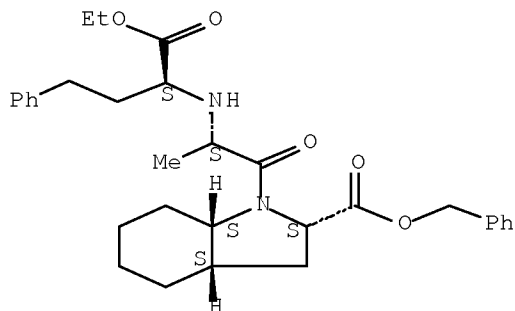
IT 83542-05-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(R\*)], 2 $\alpha$ , 3 $\alpha$ , 7 $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

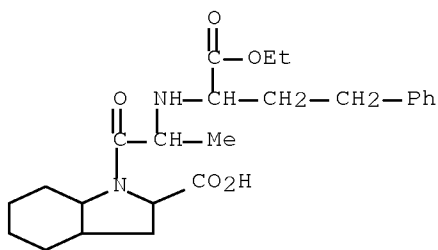


IT 80876-02-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)

RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



IT 80828-34-8P 80876-01-3P 80876-02-4P

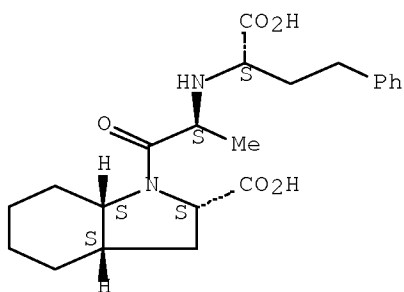
83542-06-7P 83542-08-9P 83601-86-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S, 3 $\alpha$ S, 7 $\alpha$ S)- (CA INDEX NAME)

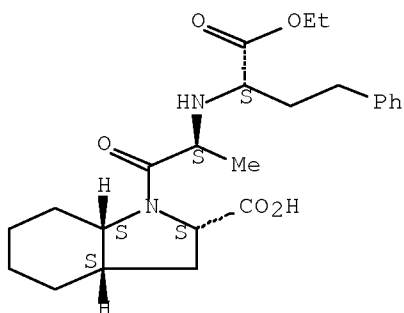
Absolute stereochemistry.



RN 80876-01-3 CAPLUS

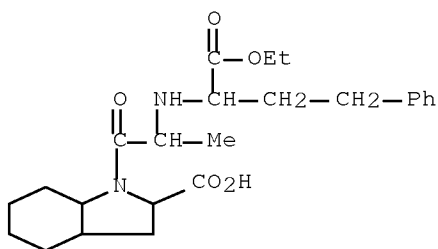
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

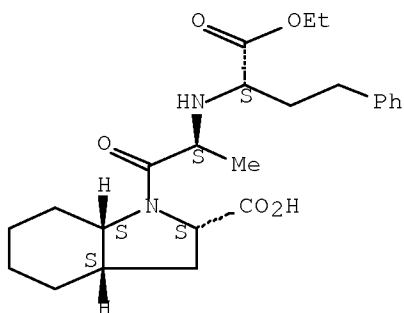


RN 83542-06-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)], 2α, 3αβ, 7αβ]]-, monoacetate (9CI) (CA INDEX NAME)

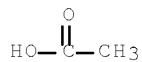
CRN 80876-01-3  
CMF C24 H34 N2 O5

Absolute stereochemistry.



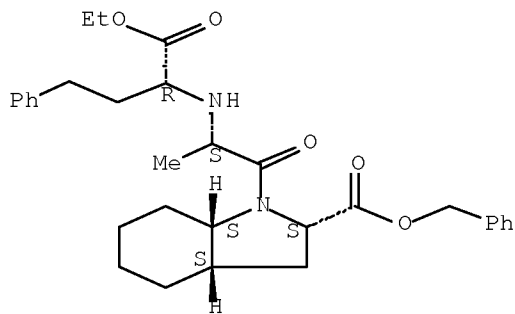
CM 2

CRN 64-19-7  
CMF C2 H4 O2

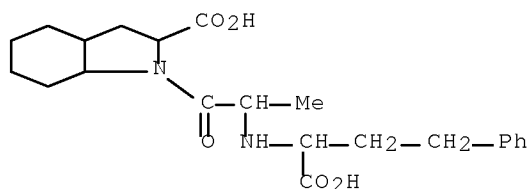


RN 83542-08-9 CAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R\*(S\*)],2 $\alpha$ ,3 $\alpha$ ,7 $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 83601-86-9 CAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



L36 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 1982:616716 CAPLUS Full-text  
 DN 97:216716  
 OREF 97:36393a,36396a  
 TI Substituted imino diacids and pharmaceutical preparations containing them  
 IN Remond, Georges; Laubie, Michel; Vincent, Michel  
 PA Science Union et Cie., Societe Francaise de Recherche Medicale, Fr.  
 SO Eur. Pat. Appl., 38 pp.  
 CODEN: EPXXDW

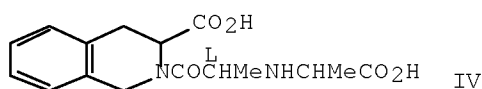
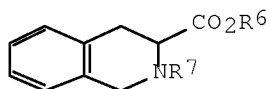
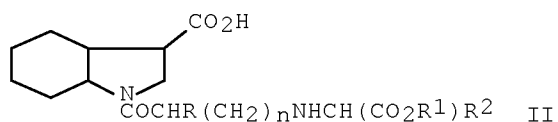
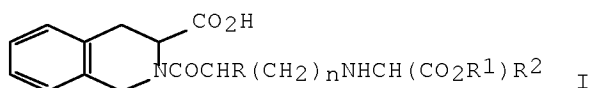
DT Patent

LA French

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 49658	A1	19820414	EP 1981-401501	19810929
	EP 49658	B1	19840613		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	FR 2491469	A1	19820409	FR 1980-21095	19801002
	FR 2491469	B1	19830513		
	FR 2503155	A2	19821008	FR 1981-6916	19810407
	FR 2503155	B2	19830701		
	IL 63940	A	19850630	IL 1981-63940	19810925
	AT 7910	T	19840615	AT 1981-401501	19810929
	FI 8103034	A	19820403	FI 1981-3034	19810930
	FI 77230	B	19881031		
	FI 77230	C	19890210		
	DK 8104343	A	19820403	DK 1981-4343	19811001
	DK 157011	B	19891030		
	DK 157011	C	19900326		
	NO 8103339	A	19820405	NO 1981-3339	19811001
	NO 160780	B	19890220		
	NO 160780	C	19890531		
	AU 8175949	A	19820408	AU 1981-75949	19811001
	AU 542611	B2	19850228		
	HU 28405	A2	19831228	HU 1981-2838	19811001
	HU 185147	B	19841228		
	SU 1153827	A3	19850430	SU 1981-3344196	19811001
	CA 1341196	C	20010306	CA 1981-387093	19811001
	JP 57091974	A	19820608	JP 1981-157367	19811002
	JP 01032239	B	19890629		
	ZA 8106844	A	19820929	ZA 1981-6844	19811002
	US 4508729	A	19850402	US 1981-308234	19811002
	US 4565819	A	19860121	US 1982-420005	19820920
	US 4616029	A	19861007	US 1984-659275	19841010
	US 4616031	A	19861007	US 1984-659276	19841010
	US 4644008	A	19870217	US 1984-659274	19841010
	US 4616030	A	19861007	US 1984-679320	19841206

PRAI FR 1980-21095 A 19801002  
 FR 1981-6916 A 19810407  
 FR 1979-30046 A 19791207  
 FR 1980-16875 A 19800731  
 US 1980-212607 A2 19801203  
 EP 1981-401501 A 19810929  
 US 1981-308234 A1 19811002  
 OS CASREACT 97:216716; MARPAT 97:216716  
 GI



AB Heterocyclic amino acid derivs. I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, (CH2)mXCHR3R4 [R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxy carbonyl; X = S, NR5 (R5 = H, Ac, CO2CH2Ph), m = 1, 2]; n = 0, 1] were prepared. Thus, (S)-phenylalanine was cyclized with H2CO to give (S)-isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/SOCl2 and then condensed with Boc-L-Ala-OH (Boc = Me3CO2C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF3CO2H to give (S)-III.CF3CO2H (R6 = H, R7 = H-L-Ala), which was treated with MeCOCO2H and then reduced by NaBH3CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypolypeptidase, kininase, and angiotensin-converting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE.

IT 82961-92-0P

RL: SEN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

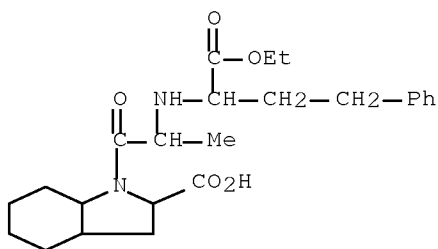
RN 82961-92-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2Z)-2-butenedioate (2:1) (CA INDEX NAME)

CM 1

CRN 80876-02-4

CMF C24 H34 N2 O5

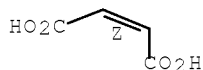


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



## **L36 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2008 ACS** **on STN**

AN 1982:492759 CAPLUS Full-text

DN 97:92759

OREF 97:15483a,15486a

TI Amino acid derivatives, compositions containing them and their use

IN Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Schoelkens, Bernward; Henning, Rainer

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 196 pp.

CODEN: EPXXDW

DT Patent

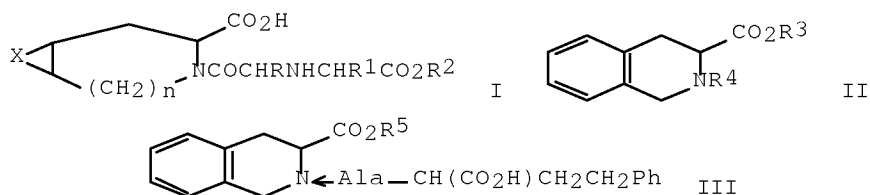
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 46953	A2	19820310	EP 1981-106535	19810822
	EP 46953	A3	19820505		
	EP 46953	B1	19891206		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	DE 3032709	A1	19820429	DE 1980-3032709	19800830
	DE 3118191	A1	19821125	DE 1981-3118191	19810508
	EP 278530	A2	19880817	EP 1988-102408	19810822
	EP 278530	A3	19890802		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 328160	A1	19890816	EP 1989-105371	19810822
	EP 328160	B1	19940504		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 48415	T	19891215	AT 1981-106535	19810822
	AT 105301	T	19940515	AT 1989-105371	19810822



FI 8102652	A	19820301	FI 1981-2652	19810827
FI 90072	B	19930915		
FI 90072	C	19931227		
HU 27874	A2	19831128	HU 1981-2478	19810827
HU 189531	B	19860728		
DK 8103835	A	19820301	DK 1981-3835	19810828
DK 169382	B1	19941017		
NO 8102933	A	19820301	NO 1981-2933	19810828
AU 8174718	A	19820311	AU 1981-74718	19810828
AU 544756	B2	19850613		
ZA 8105988	A	19820825	ZA 1981-5988	19810828
IL 63683	A	19880331	IL 1981-63683	19810828
JP 01048918	B	19891020	JP 1981-134401	19810828
US 5158959	A	19921027	US 1983-565900	19831227
US 5162362	A	19921110	US 1983-565887	19831227
ES 530715	A5	19850614	ES 1984-530715	19840316
AU 8779284	A	19880204	AU 1987-79284	19871001
AU 599151	B2	19900712		
JP 01125398	A	19890517	JP 1988-209625	19880825
JP 06078355	B	19941005		
AU 8936625	A	19891005	AU 1989-36625	19890620
AU 627741	B2	19920903		
JP 04217994	A	19920807	JP 1991-77208	19910318
JP 07121955	B	19951225		
FI 90069	B	19930915	FI 1991-4555	19910927
FI 90069	C	19931227		
FI 90532	B	19931115	FI 1991-4554	19910927
FI 90532	C	19940225		
US 5401766	A	19950328	US 1994-208443	19940309
PRAI DE 1980-3032709	A	19800830		
DE 1981-3118191	A	19810508		
EP 1981-106535	P	19810822		
EP 1989-105371	A	19810822		
US 1981-297191	A3	19810828		
JP 1982-117311	A	19820705		
JP 1982-117312	A	19820705		
OS CASREACT 97:92759; MARPAT 97:92759				
GI				



AB Amino acid derivs. I (X = fused benzene or cyclohexane ring; R, R1 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, aryl, partially hydrogenated aryl, aralkyl, heterocyclic residue; R2 = H, alkyl, alkenyl, aralkyl; n = 0, 1) were prepared as long-lasting antihypertensives (no data). Thus, tetrahydroisoquinoline II (R3 = R4 = H) was treated with ZCl (Z = PhCH2O2C) to give II (R3 = H, R4 = Z), which was esterified with Me3COH by DCC in CH2Cl2 containing 4-(dimethylamino)pyridine to give 97% II (R3 = CMe3, R4 =

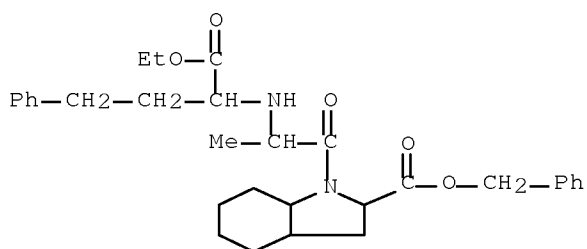
Z), which was Z-deblocked by hydrogenolysis and then condensed with Z-Ala-OH by DCC/1-hydroxybenzotriazole to give II (R3 = CMe3, R4 = Z-Ala). The latter was Z-deblocked by hydrogenolysis to give II (R = CMe3, R4 = Ala), which condensed with PhCH2CH2COCO2H and was then reduced with NaBH3CN to give isoquinoline III (R5 = CMe3), which was debutylated by CF3CO2H to give III (R5 = H).

IT 82717-98-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)

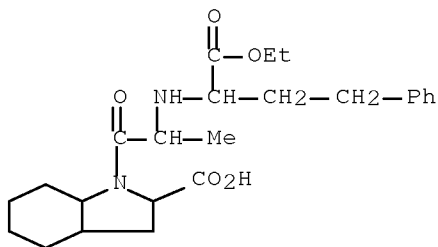


IT 80876-02-4P 82717-98-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

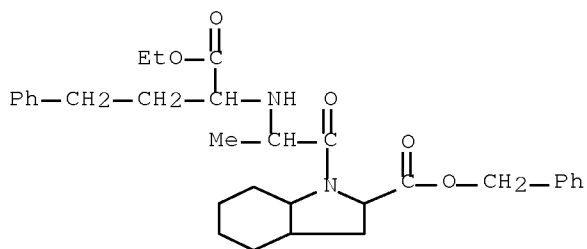
RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)



## **L36 ANSWER 111 OF 111 CAPLUS COPYRIGHT 2008 ACS**

### **on STN**

AN 1982:122630 CAPLUS Full-text

DN 96:122630

OREF 96:20133a,20136a

TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids

IN Hoefle, Milton Louis; Bobowski, George

PA Warner-Lambert Co. , USA

SO Eur. Pat. Appl., 47 pp.

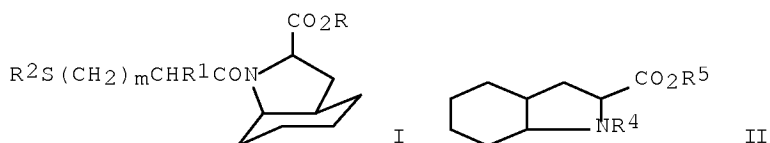
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 37231	A2	19811007	EP 1981-301243	19810324
	EP 37231	A3	19820428		
	EP 37231	B1	19870128		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4350704	A	19820921	US 1981-233940	19810217
	ZA 8101493	A	19820331	ZA 1981-1493	19810305
	EP 88341	A1	19830914	EP 1983-101990	19810324
	EP 88341	B1	19870722		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 88342	A1	19830914	EP 1983-101991	19810324
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 25243	T	19870215	AT 1981-301243	19810324
	AU 8168939	A	19811008	AU 1981-68939	19810331
	AU 543861	B2	19850509		
	SU 1246893	A3	19860723	SU 1981-3339202	19811005
	SU 1241988	A3	19860630	SU 1982-3498497	19821010
PRAI	US 1980-137106	A	19800402		
	US 1980-194307	A	19801006		
	US 1981-233940	A	19810217		
	EP 1981-301243	P	19810324		
OS	MARPAT 96:122630				
GI					



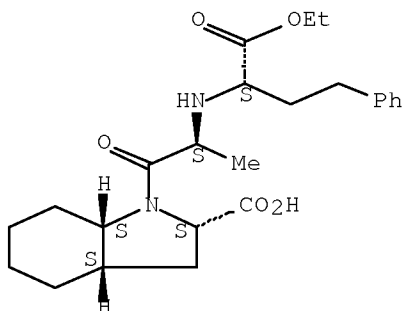
AB Indolecarboxylates I [R = H, alkyl; R1 = H, alkyl, CH2Ph; R2 = H, COR3 (R3 = alkyl, C4-9N1-201-2S1-2 heteroaryl, Ph optionally substituted with 1 or 2 F, Cl, Br, alkyl, alkoxy); n = 0, 1], useful antihypertensives, were prepared. Et indole-2-carboxylate was hydrogenated and the octahydro ester 2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ -II (R4 = H, R5 = Et) hydrolyzed to give 2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ -II (R4 = R5 = H).HCl. N-Acylating this in pyridine with AcSCH2CHMeCOCl gave 2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ -II (R4 = COCHMeCH2SAc, R5 = H) diastereoisomer A which was hydrolyzed with NH3 in MeOH to give 2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ -II (R4 = COCHMeCH2SH, R5 = H) diastereoisomer A, which had in vitro IC50 (inhibitory concentration) for angiotensin converting enzyme of 7.0 + 10<sup>-9</sup> M.

IT 80876-01-3 80923-95-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (angiotensin converting enzyme inhibitory activity of)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3 $\alpha$ S,7 $\alpha$ S)- (CA INDEX NAME)

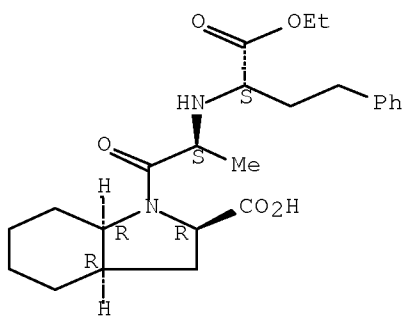
Absolute stereochemistry.



RN 80923-95-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(S\*)], 2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



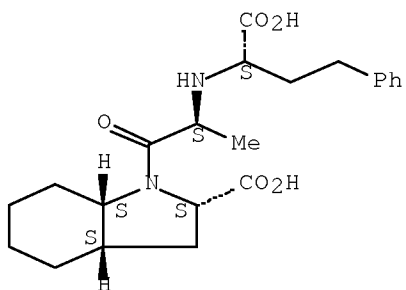
IT 80828-34-8P 80876-05-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and angiotensin converting enzyme inhibitory activity of)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

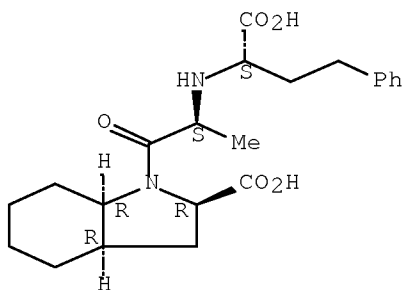
Absolute stereochemistry.



RN 80876-05-7 CAPLUS

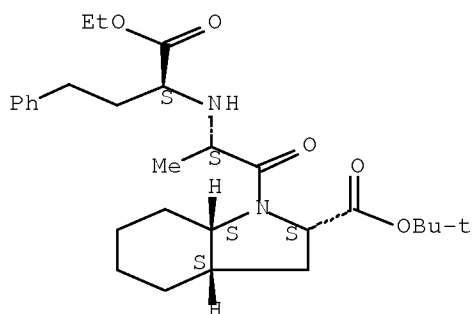
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S\*(S\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



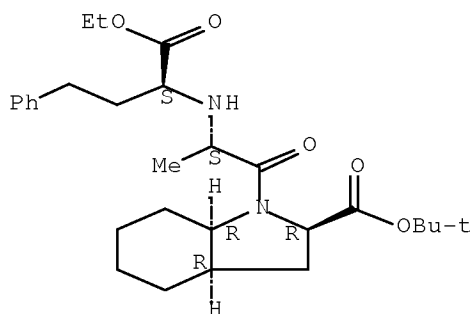
IT 80828-33-7P 80876-04-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrolysis of)  
 RN 80828-33-7 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

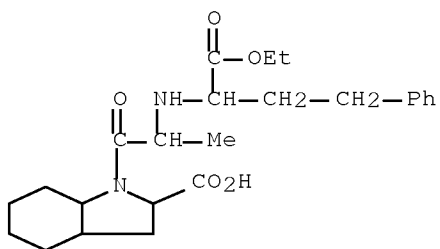


RN 80876-04-6 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2R-[1[S\*(S\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 80876-02-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)  
 RN 80876-02-4 CAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



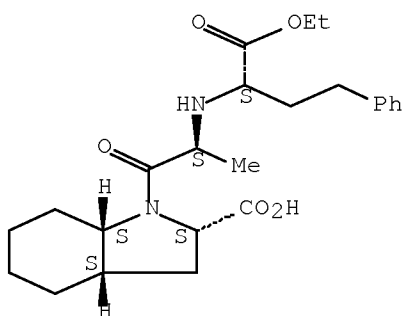
IT 80828-32-6P 80876-03-5P

RL: SFN (Synthetic preparation); PREP (Preparation)  
(preparation, saponification and hydrolysis of)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

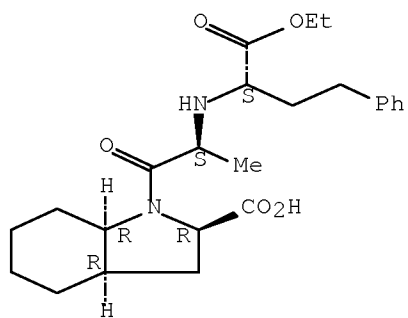


● HCl

RN 80876-03-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[S\*(S\*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> log hold

COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE

ENTRY

605.91

SINCE FILE

ENTRY

-88.80

TOTAL

SESSION

1621.66

TOTAL

SESSION

-112.80

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 10:58:51 ON 05 MAY 2008